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QUANTITATIVE DETERMINATION OF IODINE IN VIVO

by

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Roentgen diagnosis makes use of polychromatic roentgen rays. The essential information obtained is the outline and structure of organs. The anatomical details thus revealed enable the radiologist to detect certain pathological conditions. Thus, pathological conditions leading to changes in the anatomy of organs can be recognized. Also the amounts of certain elements of high atomic numbers can be roughly estimated by their increased absorption of the rays. For instance, one can estimate the amounts of certain contrast media concentrated in some organs and thus evaluate their functions. This is, however, a subjective impression requiring large amounts of contrast medium, and it cannot be as accurate as a quantitative analysis.

A true quantitative analysis of certain elements in a living body, or in a test sample of tissues or of body fluids, is possible by means of absorption measurements of monochromatic roentgen rays. New diagnostic procedures are thus made possible, since comparatively small amounts of substances can be detected and measured.

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The principle for such a system will be briefly discussed, and some examples will be given of its use in the determination of iodine, in vivo. The method, called dichromography, has been developed during the last four years. It has been described in some detail elsewhere (JACOBSON 1953, JACOBSON and MACKAY 1958, JACOBSON 1958).

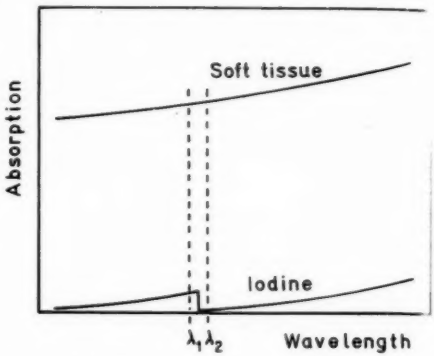

Diagram 1. Absorption as a function of wavelength for a small amount of iodine in soft tissue.

Method

Any single element or substance can be quantitatively analyzed by measuring the attenuation of one monochromatic roentgen beam according to the Lambert-Beer law. Similarly, two substances in a mixture, such as iodine and soft tissue, can be analyzed by means of two monochromatic roentgen rays. One method uses two alternating monochromatic beams, with the wavelengths λ_1 and λ_2 respectively, on either side of the absorption edge of iodine. By measuring the attenuation of the two beams, the amount of iodine traversed can be exactly calculated. This is explained by the following reasoning.

In Diagram 1 the attenuation of the roentgen rays is plotted as a function of the wavelength for soft tissue and for a small amount of iodine, as they may appear in the investigated organism. To the first approximation the attenuation of λ_2 is proportional to the amount of soft tissue only, since the absorption by the iodine is very low. Thus, the amount of soft tissue is measured by the attenuation of λ_2. The difference between the attenuation of λ_1 and λ_2 is proportional to the iodine content mainly, since the slope of the soft tissue absorption curve is moderate as compared to the sharp drop in the iodine absorption curve.

A practical system is shown in Fig. 1. Two absorption wedges, composed of the two substances in question, are maintained by servo motors in such a position that the intensities of both wavelengths remain constant at the scintillator photomultiplier unit. When the patient is put into the beam the wedges are automatically withdrawn a certain distance corresponding to the amount of soft tissue (which is the substance of one wedge) and iodine (that of the other wedge) that the beam has traversed. Thus, the displacements of the two wedges are quantitative measures of these two substances.

The amount of iodine traversed by the beam can be recorded graphi-

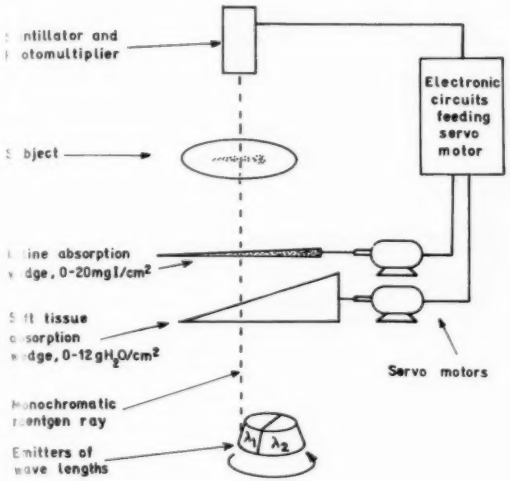

Fig. 1. Principle for method used. The movements of the absorption wedges are controlled by the electronic circuits fed by the photomultiplier unit. The two wavelengths are attenuated so that the intensities at the scintillator photomultiplier unit are kept constant. The displacements of the wedges are measures of the amounts of substances present in the subject investigated.

ally. Thus, the variations of the iodine content can be recorded as a function of time. By means of an automatic scanning procedure the spatial distribution can also be registered.

Practical tests with the equipment using a beam of 0.28 cm² in cross-section have shown that iodine in the amount of 0.2 to 0.5 mg per cm² can be detected in objects having a thickness of less than 10 cm.

Applications

Rabbits were anaesthetized with Mebumal. After an intravenous injection of Biligrafin the iodine content in various parts of the body was measured at short intervals and was also mapped out graphically during a continuous scanning.

In another set of experiments the Biligrafin secretion was studied in humans, who had been cholecystectomized, by analysis of blood, bile and urine samples.

Experiment 1. A rabbit weighing 3.5 kg was placed on its back on the examination table. The roentgen beam was made to trace a line back and forth, parallel to, and to the right of the vertebral column, between the lung, liver and lower abdomen. The amount of iodine was then con-

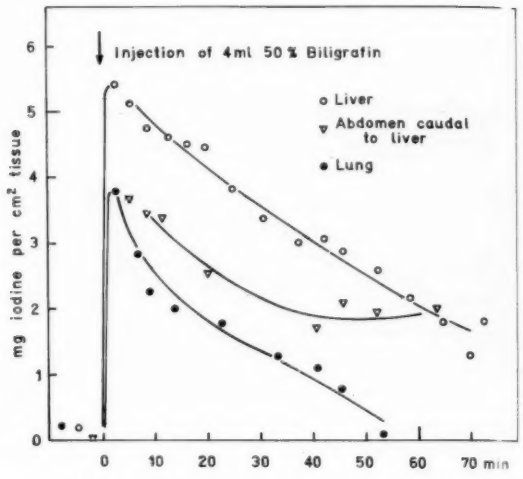

Diagram 2. Amount of iodine in the lung, liver, and lower abdomen in a rabbit after the injection of Biligrafin. The measurements were taken over three fixed spots, one over each area.

tinuously recorded before and after the intravenous injection of 4 ml 50 % Biligrafin. From the recorded curve the iodine content was plotted against time over points in the lung, liver and lower abdomen (Diagram 3). Simultaneously the thickness of the soft tissues penetrated was recorded at the same points.

Experiment 2. Another rabbit weighing 3.5 kg was placed on its side, and a surface over the upper abdomen was scanned with a traversing roentgen beam, starting caudally and going cephalad. The line density was 10 per cm and the scanning speed 0.5 cm per second. The spatial variations of the iodine content were recorded by a photographic technique after the intravenous injection of 4 ml 50 % Biligrafin (Fig. 2). Simultaneously, ink recordings were made of the absolute iodine content. From these the iodine content of different parts of the abdomen was plotted in a stereogram (Fig. 3).

Experiment 3. Three patients, operated upon one week to a fortnight earlier, because of gallstones, were selected for this experiment. At the operation the gallbladder had been removed, the common duct incised, explored and left with a drainage. In all three of them the common duct exploration was done because intravenous cholangiography prior to the operation had revealed the presence of stones. None of the patients had any signs of impairment of the liver function. The patients, weighing be-

Fig. 2. Photographic recordings of the iodine contents of the upper abdomen of a rabbit injected with Biligrafin. Light areas correspond to the presence of iodine from about 3 mg I/cm² to 7 mg I/cm², roughly corresponding to the content in the liver. The other regions, having an iodine content below this range, are black. Due to the animal's breathing during scanning, the contours of the liver are blurred and slightly irregular.

tween 60 to 65 kg. were given 40 ml 50 % Biligrafin intravenously. Samples of blood and bile were taken at 2.5 to 20 min intervals for 2.5 hours after the injection. The bile was sucked from the common bile duct by means of a negative hydrostatic pressure of 10 to 100 cm water. In order to prevent loss of bile to the duodenum the sphincter of Oddi was closed by means of 0.5 cg doses morphine given at 45 min intervals during the experiments. Urine excreted during the period of investigation was also collected. During the experiment, roentgenograms were taken of the liver in two cases. The samples of blood, bile and urine were analyzed with the dichromography method for the amounts of iodine present. The results from the three patients were in fair agreement as to the amount of Biligrafin present in the blood and the amounts excreted. In Diagrams 3 and 4, typical curves are given for the distribution of iodine during one of the experiments.

A sample of heparinized blood taken during one of the experiments was analyzed for Biligrafin in the separated red cells and the plasma. All the Biligrafin was found in the plasma.

Conclusions about Biligrafin excretion. Immediately after the intravenous injection of Biligrafin in the rabbit experiments, the amounts of iodine in the lung and the lower abdomen were about 4 mg I/cm² and in the liver about 5 mg I/cm² (Diagram 2). After this initial phase the amounts in the lung and liver decreased steadily with an almost constant difference of about 2 mg I/cm². The decrease of iodine in the abdomen was slower and changed gradually to an increase.

The initial amounts of iodine in the measured places were of the same order of magnitude as one would expect if the gross distribution of Biligrafin

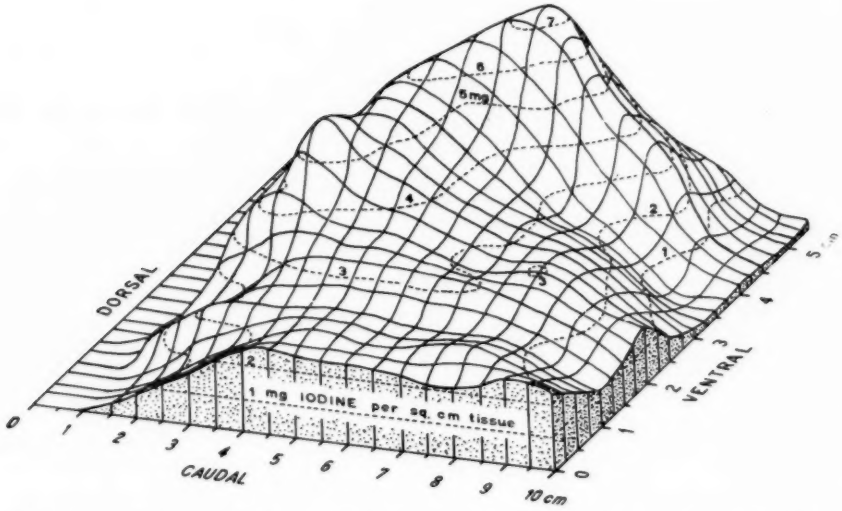

Fig. 3. Stereogram recordings of the absolute iodine content of the upper abdominal part of the rabbit made simultaneously to those in fig. 2. Each point in the stereogram is a mean value of the recordings for a picture area of about 0.24 cm².

was uniform throughout the body. (As pointed out above the soft tissue values were always measured simultaneously with the iodine content and this allowed the calculation of the distribution of Biligrafin.) The lower amount of total iodine measured in the lung and abdomen is probably partly due to the presence of air and scybala, which reduces the effective tissue volume. The difference between the amounts of iodine in the liver and the lung is rather small and constant during the excretion. This fact could be explained if one assumes that the concentrations of Biligrafin were the same in the liver tissue as in other body tissues, the amounts present in the biliary ducts excepted. This assumption is consistent with the shape of the liver in Fig. 2 and the stereogram of Fig. 3. The distribution of iodine in the liver is not uniform but concentrated in local ridges which may correspond to the biliary tree. KIMBEL and WILLENBRINK (1958) found a low content of Biligrafin in the liver of rats even after prolonged administration. Similarly, KIMBEL, HEINKEL and BÖRNER (1956) found that no appreciable accumulation of Biligrafin ocurred in the liver.

The experiments on the excretion in humans confirm the findings in the rabbit experiments. The concentration of Biligrafin in the blood, after equilibrium had been reached in about 7 min, implies that the con-

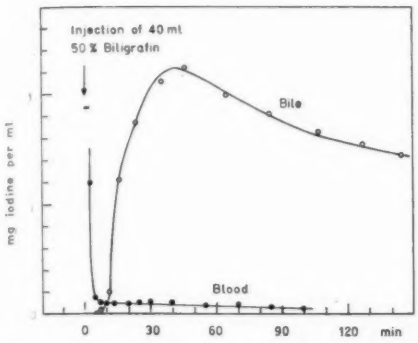

Diagram 3. Iodine concentration in blood and bile samples as a function of time after intravenous injection of Biligrafin to a patient with a common bile duct drainage.

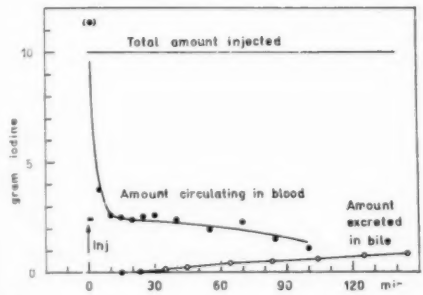

Diagram 4. Total amount of iodine present in the circulating blood and in excreted bile as a function of time after the intravenous injection of 40 ml 50 % Biligrafin in the same experiment as in diagram 3. After 2 hours 1.7 g iodine was found in the urine excreted during the experiment.

trast medium had distributed itself in a volume that corresponds to the extracellular space. This conclusion is supported by the finding that Biligrafin does not enter the red cells.

In Diagram 3 a phase shift in the curves is obtained since the bile sample obtained at a certain instant was secreted in the liver cells some 5 to 10 minutes earlier.

For liver function tests it is of interest to calculate the clearance factor for Biligrafin. Although no complete investigation has been made of this problem, the clearance in one of the patients was 16 ml whole blood per minute for the period immediately after the injection. KIMBEL and WILLENBRINK (1958) found clearance values in rats between 5 and 9 ml per minute per kg body weight.

The dichromography method should be of value for liver function tests on humans when the output from the roentgen tube has been increased sufficiently for studying thicker objects. Then it should be possible to determine the excretion capacity of the liver for compounds such as Biligrafin without access to bile samples. By scanning the patient in a direction perpendicular to the choledochus, the width of the duct and the amount of contrast medium present can be determined, and this should make it possible to obtain quantitative values for an evaluation of the liver function.

The subjective impression obtained from viewing the roentgen films of the liver region was in agreement with the curves. A concentration of 10 to 12 mg iodine per ml bile gave fairly good visibility of the bile ducts, whereas ducts containing bile with 5 to 7 mg iodine per ml could hardly be detected.

As a result of the above it seems probable that true hepatography, i. e. radiographic demonstration of the liver parenchyma, is not possible with Biligrafin. Due to the high sensitivity of the measuring method used, it is possible, however, to observe the accumulation of contrast in the parenchymal bile ducts. By such observations it is thus possible to measure and study the excretory function of the peripheral parts of the liver.

Discussion

The experiments described were performed to demonstrate one of the possible applications of the dichromography method for analyzing small amounts of specific substances in vivo. Iodine analysis is of general interest for studying the function of organs that can concentrate media containing this element. As will be reported elsewhere, preliminary studies of human thyroids show the applicability of the method for iodine metabolism studies.

Preliminary experiments on patients have shown that this method may be used to study the function of certain organs. The present equipment, however, is limited to objects under 10 cm thickness with the sensitivity mentioned above, and functions up to 18 cm with reduced sensitivity. It should be noted that only thin layers of skeletal structures, such as the rabbit thoracic wall, can be tolerated without reducing the accuracy of the method. Similarly, an appreciable depth of fat tissue simulates the presence of iodine; with 1 gram of fat per cm^2 simulating 0.5 mg iodine per cm^2.

To eliminate these disadvantages, it is planned to improve the method by using two additional wavelengths and wedges of bone salt and fat tissue. Thus, by means of four wavelengths and four wedges it might be possible to measure the following substances simultaneously: soft tissue (water), fat tissue, bone salt, and iodine. Although a recording of all four substances may not be desired in every case, the accuracy of the determination of any one of them will be improved if the system takes all four into account.

The dichromography method is primarily a means of quantitative analysis which can be performed in vivo. A reading requires approximately 1 second, and thus variations in the quantity of the substance can be correctly analyzed. The method may therefore find various applications in the field of medical research and diagnosis. By using the absorption edges of elements with an atomic number similar to iodine, or higher, a specific analysis of these elements can be made with appreciable sensitivity. The absorption edges for elements of lower atomic numbers occur at a longer

wavelength with insufficiently penetrating power for clinical use. For an analysis of these substances one is forced to employ a non-specific method, using the difference in the continuous part of the absorption coefficient curve, which will result in a lower accuracy.

By scanning procedures, as exemplified in Fig. 2, pictures can only be produced, however, with all the disadvantages previously observed in such procedures. Thus the resolution is low, and the area investigated within a certain time is limited. Such pictures, on the other hand, give information not only about the outline of an organ, but also provide a map of the quantitative distribution of the substance in question. The amounts of contrast substance that has to be penetrated for this purpose is only a fraction (less than one tenth) of that required for an ordinary roentgenogram.

Acknowledgements

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SUMMARY

Absorption measurements of monochromatic roentgen rays enable the quantitative analysis of small amounts of certain elements. After injection of Biligrafin, the iodine content in the lung, liver, and lower abdomen of rabbits was measured, and it was also determined in samples of bile, blood and urine from three cholecystectomized patients. The Biligrafin distributed itself in the extracellular space. The method, called dichromography, was found to be sensitive enough to detect 0.2 to 0.5 milligrams of iodine per cm^2 tissue. An apparatus for such measurements is briefly described.

ZUSAMMENFASSUNG

Absorptionsmessungen monochromatischer Röntgenstrahlen ermöglichen die quantitative Analyse kleiner Mengen gewisser Elemente. Nach Injektion von Biligrafin wurde bei Kaninchen der Jodgehalt der Lungen, der Leber und des unteren Bauchabschnittes gemessen; er wurde auch in der Galle, im Blut und im Urin von 3 cholecystektomierten Patienten bestimmt. Das Biligrafin verteilte sich im extrazellulären Raum. Die benutzte Methode, die Dichromographie, erwies sich als empfindlich genug, Mengen von 0.2 bis 0.5 mg Jod per Quadratzentimeter Gewebe zu entdecken. Ein Apparat für derartige Messungen wird kurz beschrieben.

RÉSUMÉ

Des mesures d'absorption de rayonnement roentgen monochromatique permette t l'analyse quantitative de petites quantités de certains éléments. La teneur en iode d u poumon, du foie et de l'abdomen inférieur de lapins a été mesurée après injection d e Biligrafin, et a aussi été déterminée dans des échantillons de bile, de sang et d'uri e provenant de malades cholécystectomisés. La Biligrafin se répartit dans l'espace extr a-cellulaire. Cette méthode, appelée dichromographie, s'est montrée assez sensible po r déceler 0.2 à 0.5 mg d'iode par cm² de tissu. Les auteurs décrivent brièvement un a p-pareil pour ces mesures.

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FROM THE NEUROLOGIC DEPARTMENT (DIRECTOR: PROF. ERIC KUGELBERG) AND THE ROENTGEN DEPARTMENT (DIRECTOR: PROF. ERIK LINDGREN), SERAFIMERLASARETTET, STOCKHOLM, SWEDEN

BILATERAL ANOMALIES OF THE MIDDLE CEREBRAL ARTERY IN RECURRENT SUBARACHNOID HAEMORRHAGE

Report of a case

by

Olle Höök and *Georg-Fredrik Saltzman*

Arteriographic evidence of intracranial vascular anomalies was found in a few cases in a series of subarachnoid haemorrhage in which no aneurysm was disclosed (Höök). One of these cases presented a unique picture of bilateral anomalies of the middle cerebral artery which, as far as we can gather from the literature, has not been previously described.

Case report

Woman, aged 47, had been well until she had a subarachnoid haemorrhage in October 1940; no focal neurologic signs were present. For some years afterwards she had had short attacks of dizziness and a sensation of heaviness in the left arm and leg. When seen in 1942 the neurologic examination revealed nothing abnormal.

Angiography (*right common carotid artery*). The carotid siphon had normal outlines. There was no filling of the anterior cerebral artery and the main branches of the middle cerebral artery were unusually narrow. In the region supplied by the lenticulo-striate arteries there were numerous tortuous, fairly large vessels which were apparently receiving

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the greater part of the blood from the main branch of the middle cerebral artery. The posterior cerebral artery was large and, in addition to its normal area of distribution, supplied large areas of the posterior parietal region. Retrograde filling of the posterior parts of the pericallosal artery was obtained through collaterals from branches of the posterior cerebral artery.

Angiography (*left internal carotid artery*). The carotid siphon had normal outlines. The anterior cerebral artery was small, but passed over in the usual way into a fairly narrow pericallosal artery. The middle cerebral artery and its branches had the same appearance as on the right side, the main branches being small, while numerous fairly large tortuous vessels were visible at the site of the lenticulo-striate arteries. The posterior cerebral artery was filled but it was not particularly large; its distribution was normal. The ophthalmic artery and its anterior ethmoidal branch were uncommonly large.

Encephalography. Apart from slight enlargement of both the lateral ventricles there were no signs of abnormality.

The patient was subsequently free from symptoms until 1958, when she had another subarachnoid haemorrhage 3 weeks after a normal partus. The initial symptom was a dull pain in the neck, and after some hours an intense frontal headache developed. She was admitted to her local hospital where she was found to have stiffness of the neck and to be slightly apathetic but was orientated with respect to space and time. The cerebrospinal fluid contained a large number of red blood cells. Neurologic examination revealed nothing else of interest. The headache subsided after a few weeks, and when discharged about 6 weeks later the patient was symptom-free.

Discussion

Small vascular deformities or variations in the vessels of the brain are by no means uncommon. Besides arterial or arteriovenous aneurysms there are other types of anomalies, such as pathologic anastomoses between the carotid and basilar arteries. The presence of the latter anomaly is due to the persistence of embryonic vascular communicating (the trigeminal, acoustic, and hypoglossal) arteries. The most common deformity of this type is the primitive trigeminal artery. Detailed descriptions of this anomaly have recently been published by KRAYENBÜHL & YAŞARGIL, and SALTZMAN.

A combination of carotid-basilar anastomoses and arterial aneurysms has been observed by MURTAGH et coll. and SCHAERER in cases of subarachnoid haemorrhage. Such anastomoses have also been encountered in patients with subarachnoid haemorrhage but without signs of arterial aneurysm (HARRISON & LUTTRELL, HÖÖK, KLOOS, SALTZMAN).

Another recently observed deformity which is apparently not particularly uncommon is infundibular widening of the proximal portion of the posterior communicating artery (SALTZMAN). Several of the patients in whom this vascular anomaly was observed had had subarachnoid haemorrhage, often without concomitant arterial aneurysm. Histologic studies in a few cases with this malformation (HASSLER & SALTZMAN) revealed changes in the vascular wall, with wide-spread media defects of approximately the same type as may be observed in arterial aneurysm.

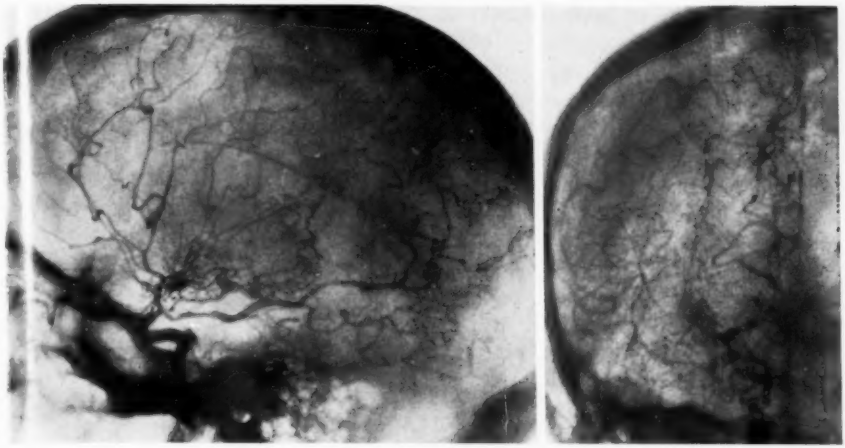

Fig. 1. Angiography via the right common carotid artery. Anterior cerebral artery not filled and main branches of the middle cerebral artery narrow. Numerous large arterial branches visible at the site of the lenticulo-striate vessels. Large posterior cerebral artery, which in addition to its normal area of distribution supplies blood to posterior parts of parietal region. Posterior portion of pericallosal artery filled through collaterals running from posterior cerebral artery.

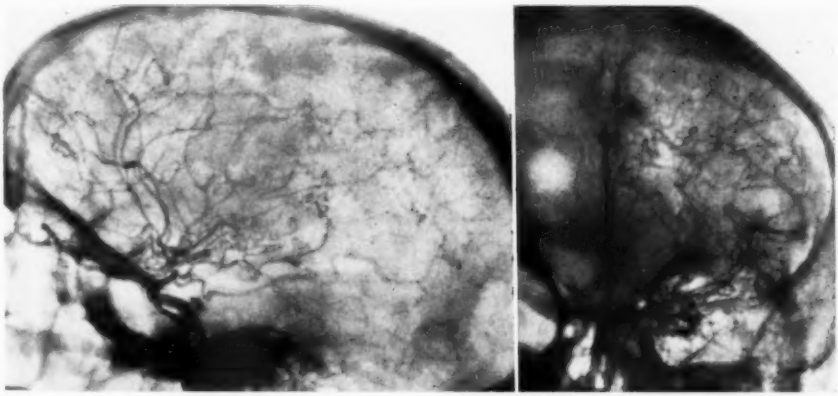

Fig. 2. Angiography via left internal carotid artery. Anterior cerebral artery narrow but continues normally into a small pericallosal artery. Narrow main branches of the middle cerebral artery. At the site of the lenticulo-striate vessels numerous large arterial branches are seen. Posterior cerebral artery is filled and supplies its normal area. Large ophthalmic artery gives off a wide anterior ethmoidal artery which supplies parts of right frontal region.

Several investigators have stressed the greatly increased incidence of vascular deformities in large series of arterial aneurysm. RIGGS & RUPP observed abnormalities of the circle of Willis in 118 out of 124 cases. FALCONER found the incidence to be about 50 %. PADGET considered that vascular deformity was twice as common in aneurysm series. WALTON noted an anomalous circle of Willis in 26 % of his cases of arterial aneurysm. It should be remembered, on the other hand, when considering these figures that small variations in the circle of Willis as well as in the anterior and posterior cerebral arteries are very common even in a normal material (ALMEIDA, KRAYENBÜHL & RICHTER, KRAYENBÜHL & YAŞARGIL, MONIZ). The most striking feature in our case was that both the middle cerebral arteries gave off a broom-like bundle of relatively large lenticulostriate branches while at the same time other branches of this artery were narrow (Figs. 1 and 2). The vascular changes involved such large areas that there was no possibility of locating any particular region as the source of the bleeding. Another remarkable finding was the system of collaterals running between the posterior cerebral and pericallosal arteries on the right side; a similar observation has been reported by HAUGE and other authors in connection with thrombosis of the internal carotid artery. We have also obtained angiographic demonstration of a circulation through this collateral system in another case in which transient contraction of the internal carotid artery and all its branches developed after a head injury.

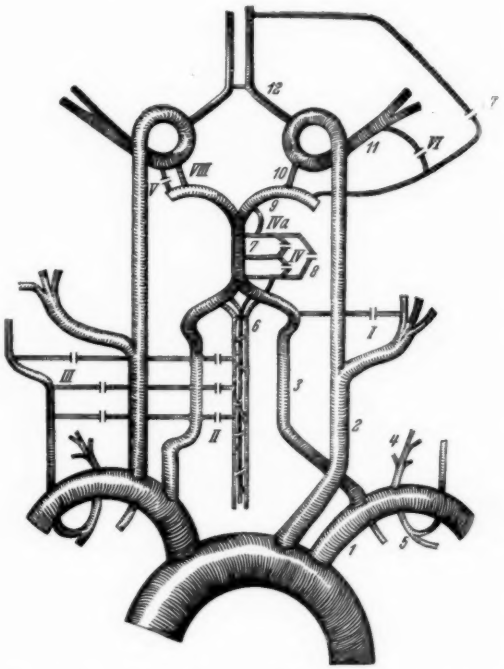

Fig. 3. The Killian-Krayenbühl-Yaşargil schema showing anastomoses between the carotid and vertebral systems. From KRAYENBÜHL & YAŞARGIL. See References. (Courtesy of H. Krayenbühl and G. Thieme Verlag.)

No filling was seen of the anterior cerebral artery on the right side.

D fective filling of this artery and its branches need not necessarily in ply that an anatomic obstruction to the circulation is present (WICK-B M, RUGGIERO). The collateral system which had formed between the p terior cerebral and pericallosal arteries, and which was found to be u hanged at both examinations, suggests, however, that in our patient a organic obstruction was indeed present. The large ophthalmic and a erior ethmoidal arteries on the left side in all probability also played a art in supplying the area which normally receives its blood through th anterior cerebral artery on the right side.

With regard to the development of the collateral system between the ve tebral and carotid arteries the reader is referred to the schema worked ou by KILLIAN and further elaborated by KRAYENBÜHL & YAŞARGIL (F g. 3). The collateral arteries in our case belonged to type VII in this sch ma.

SUMMARY

A case of multiple intracranial vascular anomalies with recurrent subarachnoid haemorrhage is described and the relationship between different vascular anomalies and subarachnoid haemorrhage is discussed.

ZUSAMMENFASSUNG

Ein Fall mit multiplen intrakraniellen Gefässanomalien und rezidivierenden Subarachnoidalblutungen wird beschrieben. Die Beziehungen zwischen verschiedenen Gefässmissbildungen und Subarachnoidalblutungen werden besprochen.

RÉSUMÉ

Les auteurs décrivent un cas d'anomalies vasculaires intracraniennes multiples avec hémorrhagies sous-arachnoïdiennes récidivantes et ils examinent les rapports entre les hémorrhagies sous-arachnoïdiennes et diverses anomalies vasculaires.

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PERCUTANEOUS LIENO-PORTAL VENOGRAPHY IN THE DEMONSTRATION OF LIVER MASSES

by

Sture Stattin

The surface of the liver can usually be fairly well outlined in conventional films but earlier attempts to examine the structure of the liver roentgenologically have not proved very successful. Various contrast media have been used. Some of these, such as Thorotrast and Angiopac, are retained in the reticulo-endothelial system of the liver, while others, such as the halogenated fat tested by OLSSON and EKMAN, are excreted by the liver cells. These agents, however, have either not given satisfactory results or have produced severe toxic side-effects. Sooner or later they have all been abandoned.

During the past ten years interest has been directed towards the use of various angiographic methods aimed at contrast-filling of the hepatic artery, the hepatic veins, or the portal vein, with their branches. When using these methods to study space-occupying lesions it is essential that the small vessels including the sinusoids are also filled with contrast medium sufficiently highly concentrated as to cause more or less homogenous opacity of the liver. To obtain such a concentration at aortography the amount and concentration of the medium injected has to be so great that the risk of causing renal damage would be considerable. The contrast medium can, however, be injected directly into the hepatic or coeliac artery, e. g. by means of a catheter inserted percutaneously, and with

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this method it is possible to obtain sufficient filling of the sinusoids to produce almost homogenous opacity of the liver. ÖDMAN has shown that fairly large quantities of contrast medium may be injected into the coeliac or hepatic artery without causing obvious damage to the organs supplied by these arteries. It is also possible, it is true, to obtain filling of the portal vein at coeliac arteriography, but as far as can be judged from ÖDMAN's paper, this is not so in all cases, and homogenous opacity of the liver with accompanying filling of the portal vein can usually not be obtained at the same examination. Considerably increased density of parts of the liver may also be achieved by means of retrograde injection of contrast medium into the hepatic veins. A disadvantage of this method is, however, that it does not permit a study of the changes in the portal blood flow.

With lieno-portal venography, on the other hand, it is possible both to study the blood flow through the liver and to produce an increased density of the liver. Contrast examination of the portal vein was first performed at operation after direct puncture of the vein itself or one of its tributaries. Later it was found that satisfactory filling of the portal vein could be obtained if contrast medium was injected into the spleen. This method, usually called percutaneous lieno-portal venography (p.l.p.v.), seems to have been used mainly for studying the hemodynamic conditions. There are, however, cases reported in which this method has also proved to be useful for demonstrating space-occupying lesions.

Since 1955 we have used p.l.p.v. in cases in which mass lesions, especially metastases, have been suspected. The technique has been described in detail in several reports (1, 5) and the one we use does not differ much from these descriptions. A preliminary film may be useful to determine the size and position of the spleen, but we have found that careful percussion is often more helpful for this purpose, unless the patient is very obese. Exact localisation of the spleen is facilitated by distending the stomach with gas (the patient is given sodium bicarbonate and tartaric acid by mouth before the examination), which is also an advantage in the main examination as the left lobe of the liver shows up better.

We do not use any particular landmarks for the puncture, but vary our procedure according to the size and position of the spleen; the smaller the spleen, the further back the puncture should be made. In practically all cases included in this report the spleen was not enlarged, that is, it was not more than 16 cm long as measured in the film. We puncture the spleen with a 10 to 15 cm needle of 1.5 mm outer diameter under local anesthesia and with the patient supine; in some cases the patient is examined both in the supine and prone positions. During and after the

puncture the patient is instructed to keep his breathing as shallow as possible and as soon as there is a free drip of blood from the needle, the contrast medium is injected. If we are uncertain about the position of the needle, this is checked in a control film or by fluoroscopy with an image-intensifier after the injection of a few millilitres of the medium.

As contrast medium we have used both Umbradil 50 % and Triurol 50 % in the first cases, but later we have employed Hypaque 45 %, 30 ml being injected in each instance. Films are taken with an automatic cassette changer, the first one at the beginning of the injection and the others every two seconds afterwards, generally eight films in all. Immediately after the injection is completed the needle is withdrawn. Because the contrast medium is heavier than the blood, in many cases only the declivous branches become filled and, for a complete examination, injection with the patient both in the supine and prone positions is necessary. At the time when the examinations in this material were performed, not much was known about the effect of the contrast medium on the liver parenchyma, and for that reason we did not feel justified in using a higher concentration or a larger quantity of the medium, and we did not repeat the injection in more than a few cases. We have not noticed any obviously injurious effect of the contrast medium in the doses used. We have recently used Urografin 60 %, which has produced better contrast without causing any increased discomfort to the patients in the cases examined.

Eighty examinations were performed during the years 1955—1957. Partial or complete failure occurred in 7 cases as in 2 of these all the contrast medium was deposited outside the spleen and in 5 there was only faint filling of the splenic and portal veins and practically none in the intrahepatic branches of the portal vein. In 17 cases operation or autopsy was performed within two weeks after the examination (in 6 of them 2 to 5 days following it). Autopsy never revealed any lesion in the spleen that could be ascribed to the p.l.p.v., not even in a case examined two days after the roentgen examination. Operation four days later in one case disclosed a small amount of dark brown fluid in the abdominal cavity, but in none of the other cases operated on were any signs of hemorrhage observed in the abdomen. In one case there was a transient pleural reaction, probably caused by the needle, but no complications were observed in the other cases. We have the same experience as other authors that the patients suffer only mild discomfort during the examination.

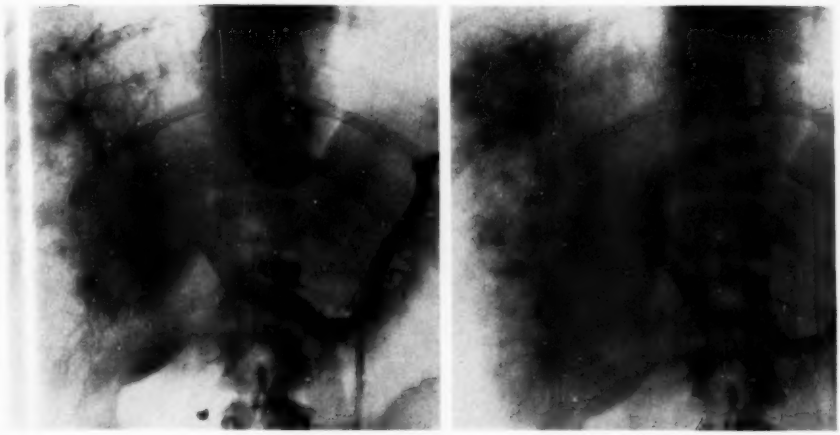
The present study includes 50 cases in which the indication for the examination was probable metastasis or a similar expanding lesion in the liver. In most of the cases a primary tumor had already been discovered elsewhere, and in the other cases the clinical signs indicated the presence

of a mass in the liver, although no primary tumor had been found. In 42 of the 50 cases autopsy or operation was performed within 2 days to about 3 months after the roentgen examination. In 27 of these, changes considered to be caused by tumor infiltration were found. In 23 cases the tumor diagnosis could be verified (metastases in 17 cases, primary hepatic carcinoma in 4, 1 echinococcus cyst, and in 1 case infiltration with degenerative tissue, which was not cirrhotic but of an obscure nature). In 4 cases the changes observed proved to be caused by hepatic cirrhosis. Of the 15 cases interpreted as normal, the liver in 12 appeared normal at operation or autopsy. In the other 3 cases, however, metastases were found; in 2 of these there were pinhead-sized metastases on the surface of but none inside the liver, and in the third case there was a large secondary deposit of a melanosarcoma close to the anterior surface of the liver, but no other metastases. Finally, in the remaining 8 of the 50 cases neither operation nor autopsy was performed and thus the conditions were not verified directly. The films in all these cases were interpreted as normal. On 'follow-up' six months to a little more than three years after the roentgen examination seven of the patients had no signs to suggest liver disease. The eighth patient could not be traced. In the 23 cases in which the findings were abnormal, the mass lesions were spread out over the liver, the only solitary tumour found being the echinococcus cyst.

Expanding lesions in the liver may be expected to produce the following changes: 1) vascular displacement, 2) vascular occlusion with resulting disturbance of the hemodynamic conditions, and 3) defects in the homogeneous contrast-filling of the liver.

Discussion

Vascular displacement. Malignant tumors are hardly likely to displace the blood vessels to any great extent, both primary and secondary growths in the liver tending to invade the vessels, especially the veins, rather than displace them. Marked displacement may be expected only in mainly expanding lesions such as cysts and abscesses. It is essential to approach the interpretation of the displacement of the vessels with a good knowledge of their normal course and variations. HJORTSJÖ, among others, has made a very thorough examination of the anatomy of the portal system. We have also obtained films in cadavers after filling the portal circulation with contrast medium. Normally there are only relatively small variations in the course and manner of ramification of at least the major branches of the portal vein. As mentioned above, it is not certain that all the vessels can be filled with one injection but exact knowledge of the normal anatomy will generally render it possible to determine to which main stem the filled branches belong.



a b

Fig. 1. Metastases from mammary cancer. a) 6 seconds after injection. Stretched and distorted vessels in the right lobe of liver. Comparatively few branches are given off from the middle part of the ventral main stem of the portal vein. These minor branches, which are filled with contrast medium of low density, in turn give off very few branches. Abrupt termination of contrast filling, slow filling and slow emptying of some of the branches. Retrograde filling of tributaries to the splenic vein. Left main stem not filled. b) 10 seconds after injection. Liver irregularly filled, many defects, in some places coalescing into large areas.

The general course of many of the branches of the portal vein is in a sagittal plane. They are thus seen in an orthograde direction in an a.p. view and are consequently not possible to interpret. If the patient is turned slightly or the liver rotated, e. g. by ascites, the branches may take another course in the film and give the impression of being displaced. As the vessels are distributed in three planes, films in two planes would be necessary for a complete interpretation. It is, however, practically impossible to obtain satisfactory true lateral films in most cases because of the high density, and furthermore, they would be difficult to interpret because so many branches would be superimposed. The difficulties caused by the sagittal course may to some extent be eliminated by obtaining stereoscopic or oblique views. This necessitates, however, either several injections of contrast medium or technical equipment which allows the beam direction in relation to the patient to be altered during the examination; this will mean the employment of two tubes or the rotation of the patient during the examination.

From what has been said above it is apparent that a major displacement of the vessels can be demonstrated only in rare cases. Small lesions scattered over a large area of the liver, on the other hand, may distort the delicate architecture of the vessels, and instead of presenting a pattern

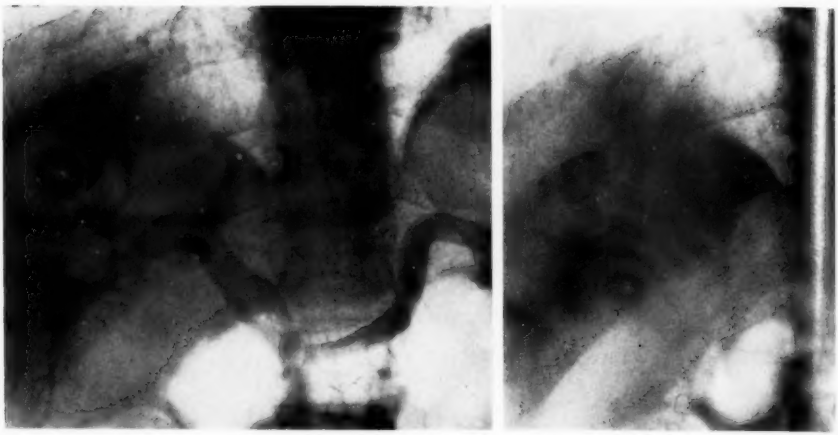


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Fig. 2. Metastases from rectal carcinoma. a) 2 seconds after injection. The contrast filling terminates abruptly in the right main stem. b) 4 seconds after injection. Large defect corresponding to the occluded branch.

of regular waves the small vessels have a stretched, rigid, and distorted appearance and pursue angular or arcuate courses. Displacement of this type may be difficult to recognise and furthermore, similar changes may also be observed in cirrhosis of the liver. As will be discussed later, however, the vessels, at least in advanced cases of cirrhosis, have a rather typical appearance. (See Fig. 5.)

Vascular occlusion with resulting disturbance of the hemodynamic conditions. As mentioned, the hepatic and the portal veins may at an early stage be invaded by malignant tumour tissue, which together with thrombi may more or less obliterate their lumen. Such occlusion may be demonstrated directly or indirectly by p. l. p. v.

Occlusion is directly evident as a more or less abrupt termination of the contrast filling in one or several branches of the veins or so that in parts of the liver only major branches appear contrast filled, the minor branches being to a great extent obliterated (Figs. 1, 2, and 4). The apparently abrupt termination of peripheral branches must be interpreted with caution, however, as such appearances may be produced if a vein running in the frontal plane suddenly veers off forwards or backwards and is shown lying in an orthograde direction; as a rule, however, the distal part of such a vessel is usually increased in density. The occlusion is not necessarily situated exactly where the contrast medium is halted

Fig. 3. Primary carcinoma of liver. 4 seconds after injection. Only the proximal part of the splenic vein is filled. Numerous tortuous vessels are filled in a retrograde direction. A further examination gave the same result. At autopsy both the splenic and portal veins were patent.

but may lie further peripherally. Thus in 3 of our cases the filling of the splenic vein ceased about ten centimetres proximal to the porta hepatis, and no medium entered the main trunk of the portal vein or its branches in the liver; some of the other tributaries to the portal vein were filled in a retrograde direction. In 1 of these cases a further examination gave the same result (Fig. 3). At autopsy, 2, 7, and 30 days later, respectively, the liver was seen to be almost entirely infiltrated with tumour tissue. In all 3 cases a number of enlarged nodes, infiltrated with carcinoma, were found in the porta hepatis, but in one of them only the portal vein was slightly compressed; both the portal and the splenic veins were otherwise quite normal and had patent lumina containing no thrombi. It is thus not always possible to differentiate between extrahepatic and intrahepatic obstruction at lieno-portal venography.

The indirect consequences of obstruction may be evident as a disturbance of the hemodynamic conditions. If there is widespread infiltration of the liver, or if the portal main stem or the major intrahepatic portal branches are occluded, the other tributaries to the portal vein may become contrast filled in a retrograde direction. If the obstruction is less and mainly restricted to a part of the liver, this may result only in a slow passage of the contrast medium in the affected regions with delayed filling and emptying of the vessels, as well as low contrast density caused by dilution of the contrast medium (Figs. 1 and 4). It must, however, be borne in mind that poor and incomplete filling of the vessels in a certain part of the liver may be due only to the usually higher density in the

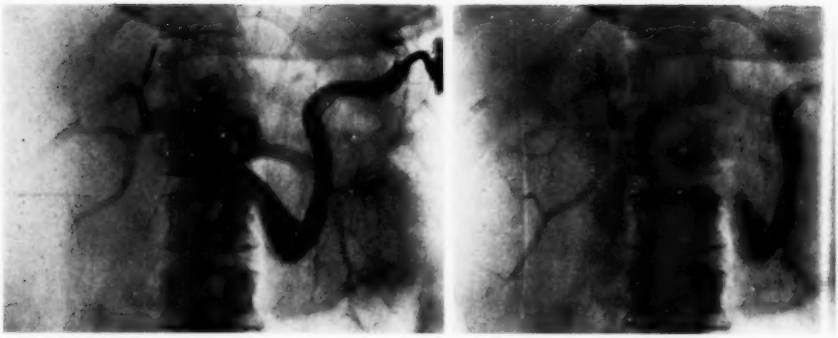

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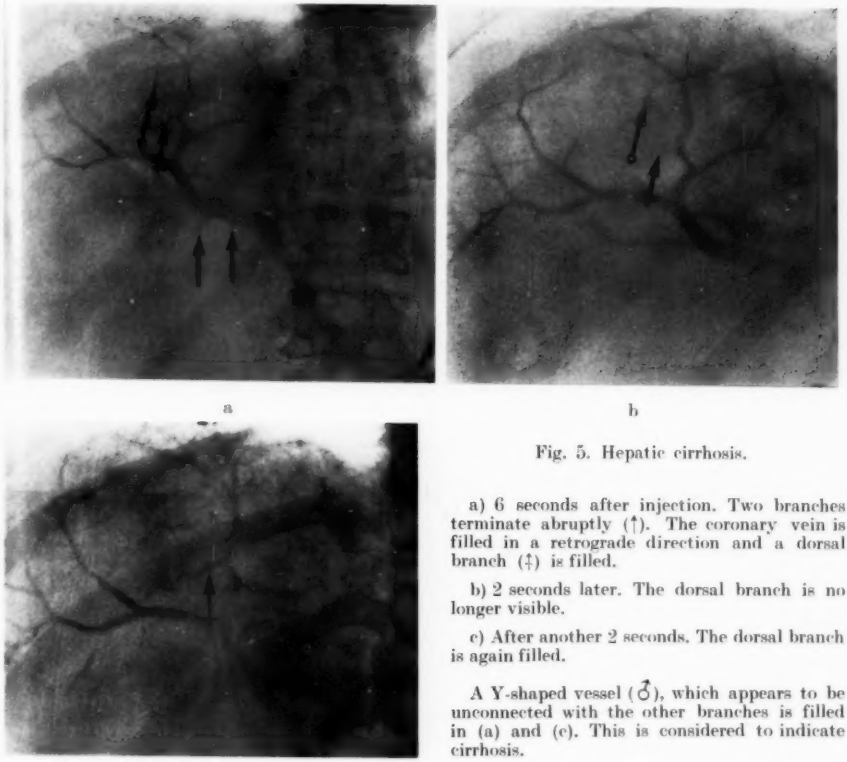
Fig. 4. Metastases from a melanosarcoma. a) 4 seconds after injection. The medium has reached the peripheral branches in the left lobe. Only a few major branches are filled in the right lobe. b) 10 seconds after injection. In the right lobe sparse, stretched and distorted vessels remain filled with contrast medium of low density when the filling of the left lobe has begun. The medium terminates rather abruptly in a dorsal branch (arrow) which remains filled after the others have emptied.

declivous vessels; to ascertain the cause for certain it may be necessary to carry out examinations in both the prone and supine positions. As the circulation rate varies within fairly wide limits, we have not tried to measure it exactly in the splenic vein, portal vein, or in the liver, and only rates deviating markedly from the normal have been registered. Thus in one case the main trunk of the right lobe had barely become filled by the time the contrast medium had reached out into the most peripheral branches in the left lobe (Fig. 4).

Defects in the homogenous filling of the liver. If a sufficient quantity of a concentrated contrast medium is injected it is possible to obtain more or less homogenous filling of the liver in the phase in which the medium has reached out into the liver sinusoids; in the parts infiltrated by tumor tissue there will be no such filling because the sinusoids are obliterated. Such defects usually appear as scattered and small, more or less rounded translucent areas (Fig. 1). In some cases, however, a fairly large part of the liver has a lower density (Figs. 1 and 2). Sufficient opacity to allow certain evaluations was obtained in 12 of our cases only, and in 7 of these, defects could be demonstrated. It seems very likely that had a higher concentration of contrast medium been used, sufficient opacity to allow safe interpretation would have been obtained in more cases.

The opacity obtained with the contrast medium also facilitates the interpretation of the size and shape of the liver; in 6 cases the lower surface definitely appeared to be uneven.



a b c

Fig. 5. Hepatic cirrhosis.

a) 6 seconds after injection. Two branches terminate abruptly (↑). The coronary vein is filled in a retrograde direction and a dorsal branch (↕) is filled.

b) 2 seconds later. The dorsal branch is no longer visible.

c) After another 2 seconds. The dorsal branch is again filled.

A Y-shaped vessel (⃗), which appears to be unconnected with the other branches is filled in (a) and (c). This is considered to indicate cirrhosis.

Differential diagnosis

Changes of a similar kind to those described may also be found in conditions of another nature, notably hepatic cirrhosis. Thrombosis is common in cirrhosis, and accordingly occlusion predominantly of the peripheral intrahepatic portal branches may occur, with resulting portal hypertension and stasis. In advanced cases the contrast filling may terminate in the portal main stem or in the splenic vein although these vessels are patent, and it will be impossible to determine the cause of the obstruction. In tumor cases with their rapid progression the portal hypertension is usually less marked than in liver cirrhosis, which is a more chronic disease. Accordingly there is less retrograde filling of the other tributaries to the portal vein in the tumor cases; in our material we

have never observed oesophageal varices and the spleen has not bee pathologically enlarged.

As we have examined patients with liver cirrhosis almost exclusivel in the late stages as a prelude to porta-cava shunt operations, we have bu little personal experience of portography in the less advanced stages o cirrhosis in which the intrahepatic branches are contrast filled. Accordin to reports in the literature, however, fairly characteristic changes in th intrahepatic branches may be found in hepatitis and in the earlier stag of cirrhosis.

WANNAGAT, who studied the portal circulation by means of laparoscopi splenoportography, describes some of these changes as "Gefässabschnü rungen und Gefässabbrüche und daneben kolbenähnliche Gefässauswei tungen von fleckigem Aussehen, in der das Kontrastmittel staut. Bei Zunahme der Veränderungen werden die Abbrüche sehr zahlreich und so massiv, dass örtlich der Eindruck entsteht, komma- oder Y-förmige Gefässabschnitte zu sehen, die keinen Zusammenhang mit dem eigentlichen Gefässbaum haben". Similar changes have been observed by us in a case of verified cirrhosis, in which one of the major branches in the right lobe terminated abruptly although the cause could not be determined (Fig. 5).

BERGSTRAND among others has pointed out the mottled and irregular appearance of the cirrhotic liver in the phase in which the contrast medium has just begun to pass over to the sinusoids. In these cases the phenomenon is probably due to the fact that the obstruction is of different degrees in different parts of the liver, the medium reaching out into the sinusoids in some places but not in others. This mottling appears in an earlier phase and is not so regular and well defined as the tumour defects in the homogenously filled liver described above.

Conclusions

The material presented indicates that it is usually possible to detect extensive masses in the liver by means of percutaneous lieno-portal venography. The only roentgenographic sign which seems to be pathognomonic of these lesions is defects in the late phase when the liver is homogenously filled with contrast medium. Abrupt termination of intrahepatic branches of the portal vein and changes indicating obstructed flow in some parts of the liver are also characteristic, although these may be seen in hepatic cirrhosis as well. When the examination is performed with the patient in the supine position, the ventral branches of the portal vein in the right lobe and all the branches in the left lobe are often only incompletely filled with contrast medium of low density; in such cases the examination should be continued with the patient prone.

SUMMARY

The value of percutaneous lieno-portal venography in the diagnosis of expanding l sions in the liver has been studied in a material including 26 verified cases of tumor, ı ainly metastases. More or less typical changes were found in practically all the cases. ' hese changes are described and their significance discussed.

RÉSUMÉ

L'auteur a étudié, sur une série comprenant 26 cas vérifiés de tumeurs, en majorité es métastases, la valeur de la spléno-portographie percutanée pour le diagnostic des tumeurs intra-hépatiques. Il a trouvé, dans pratiquement tous les cas, des modifications plus ou moins typiques. Il les décrit et examine leur intérêt.

ZUSAMMENFASSUNG

Es wurde die Verwendbarkeit der porto-lienalen Venographie in der Diagnosestellung von expandierenden Lebererkrankungen studiert. Das Material bestand aus 26 verifierten Tumoren, hauptsächlich Metastasen. In fast allen Fällen wurden mehr oder weniger typische Veränderungen gefunden. Diese werden beschrieben und ihre Bedeutung diskutiert.

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ROENTGEN DIAGNOSIS OF URETEROCELE AND SOME IMPEDING FACTORS

by

Arne E. Nilson

The cystoscopic diagnosis of ureterocele may under certain circumstances present difficulties, as has been pointed out by HELLSTRÖM (1932), and others. The correct diagnosis may be overlooked in the presence of a very large ureterocele which materially alters the topography of the bladder. Minor ureteroceles, which are raised above the normal level of the mucous membrane, only by a peristaltic wave in the ureter, may escape detection if the period of observation is a short one and happens to coincide with a period when dilatation is absent. But the prospects of urographic identification are favourable in such cases. The large ureterocele, usually associated with diminished or inhibited excretion of contrast material on the involved side, then appears as a filling defect in the bladder. The small ureterocele in which fluctuations are few may well be demonstrated in a film exposed after compression is discontinued, in which case the accumulated contrast medium on evacuation may distend the utererocele for a longer period than otherwise occurs.

Urography can then be a valuable adjunct to cystoscopy, not only for the investigation of the upper urinary tract but also for the diagnosis

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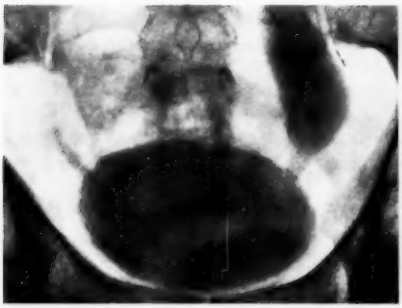

Fig. 1. Left ureter appreciably dilated above an intramural stricture. Stone in the pelvic ureteral segment. Although cystoscopy had revealed the presence of a left ureterocele, urography failed to demonstrate it.

Fig. 2. Despite incision, a ureterocele was seen cystoscopically to be half the size of a finger tip but it is not perceptible in the roentgen film. The shallow filling defect around the ureteral orifice possibly represents a collapsed ureterocele.

proper. It may therefore be of interest to consider the conditions necessary for the urographic diagnosis of ureterocele. RUDHE in 1948 described the features distinguishing the condition from hypertrophy of the prostate in cases of large ureterocele associated with inhibited excretion. Other difficulties in the roentgen diagnosis of ureterocele do not appear to have been discussed in the literature. The author has observed four cases which may serve to exemplify some of the factors impeding the roentgenographic demonstration of the condition.

For urography to make possible the demonstration of a ureterocele, the relationship between the in- and outflow of contrast material must be such that the cyst-like portion of the ureter is distended; there

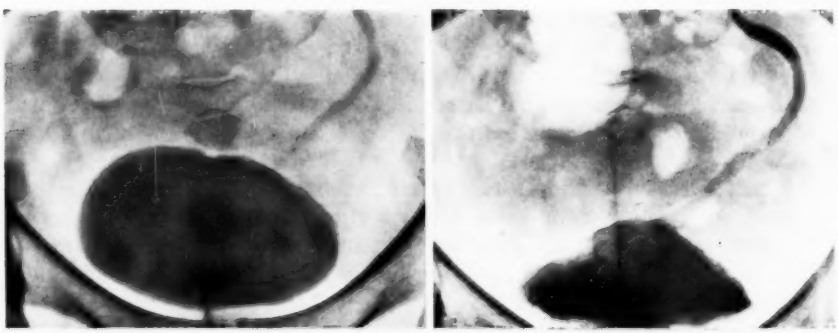

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Fig. 3. a) Inflammatory swelling of the bladder wall on the left side; no ureterocele visible. b) The inflammatory bladder changes have subsided; a ureterocele is now evident.

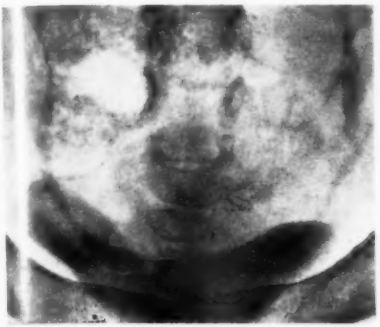

Fig. 4. After excision of a myomatous and enlarged, dextroflexed uterus, a ureterocele is contrast-filled on the right side.

must be no changes in adjacent structures which mechanically limit this distension.

If these conditions are not fulfilled, urography may fail to produce a diagnosis, as is illustrated in Fig. 1. A severe intramural stricture led to appreciable distension of the ureter and prevented the contrast medium from flowing into the ureterocele. This agrees well with the limp sac which was noted cystoscopically.

Fig. 2 shows the roentgen appearances two years after incision of a ureterocele. Although cystoscopy revealed the ureterocele still to be present, the appearances at urography were not typical. It may be that the incision had induced free drainage so that the ureterocele never became distended. Another sign of the improved drainage was that the earlier dilatation of the upper urinary tract had decreased at the time of the latest examination.

Fig. 3 illustrates how an inflammatory swelling of adjacent bladder mucosa temporarily may prevent the urographic diagnosis, probably by constituting a mechanical obstruction to the distension of the ureterocele. Nor did cystoscopy demonstrate ureterocele at that time. The ureterocele had been identified by both methods of examination on earlier as well as later occasions.

A mechanical obstruction to distension of the ureterocele may also be situated outside the urinary bladder. Fig. 4 shows a case of this type in which the ureterocele on the right side was perceptible urographically only when a myomatous, dextroflexed uterus, the size of a child's head, had been excised; this had earlier flattened the right portion of the bladder.

Conclusions

If urography is to be diagnostic, the film must be obtained when the ureterocele is distended with contrast medium. A relative decrease in the flow to or increase in the flow from the ureterocele may prevent this distension, as may also limitations of space.

SUMMARY

The factors which prevent or improve the roentgenologic demonstration of ureterocele are discussed on the basis of four illustrative cases.

ZUSAMMENFASSUNG

Unter Zugrundelegung von 4 illustrativen Fällen werden die Faktoren diskutiert, welche den röntgenologischen Nachweis einer Ureterocele verhindern oder erleichtern.

RÉSUMÉ

Se basant sur quatre cas, l'auteur examine les facteurs qui empêchent ou qui favorisent la mise en évidence radiologique de l'urétérocèle.

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ARTERIOGRAPHIC FINDINGS IN CORONARY SCLEROSIS

by

L. Di Guglielmo

The normal arteriographic appearances of the coronary arteries in living human subjects was discussed in some of our previous papers, special attention being then devoted to the study of anatomical variations and their relation to pathologic changes. The purpose of this paper is to describe the morphology of these arteries at different ages, and particularly to illustrate the features of coronary sclerosis.

Our experience is so far based upon an investigation of 549 patients, suffering from congenital or acquired heart disease, who were submitted to 658 examinations using contrast media, i. e. 305 thoracic aortographies and 353 angiocardiographies after injection into the right ventricle or pulmonary artery.

As regards the methods used in these examinations, reference should be made both to JÖNSSON's and to our own (DI GUGLIELMO & GUTTADAURO) previous papers. I wish to add, however, that thoracic aortography is the method of choice for the demonstration of the coronary arteries.

In a recent paper dealing with coronary arteriography in dogs, DOTTER and FRISCHE (1958) have apparently misinterpreted our data (DI GUGLIELMO and GUTTADAURO 1952) and conclude that thoracic aortography

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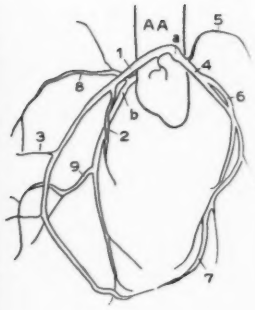


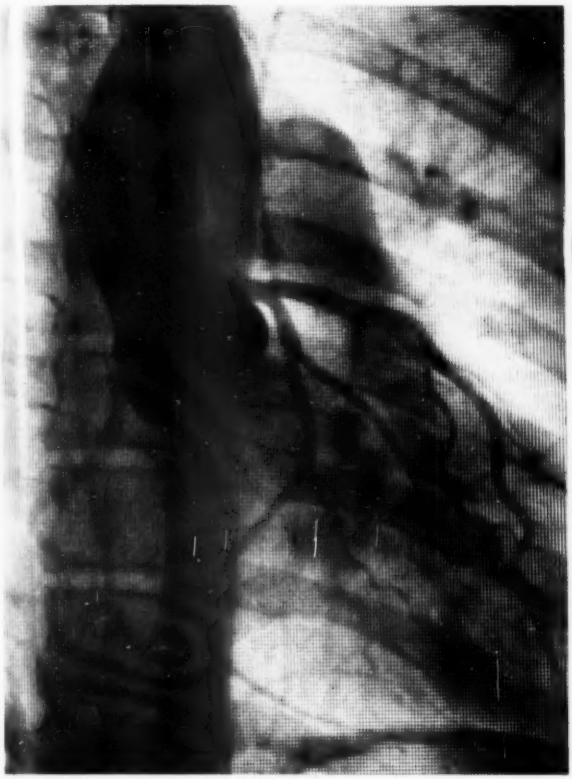
AA — ascending aorta, a — left coronary artery, 1 — anterior interventricular branch, with (2) left and (3) right branches, 4 — circumflex branch, 5 — branch to the left atrium, 6 — branch to the obtuse margin, 7 — posterior interventricular branch, b — right coronary artery, 8 — right conus branch, 9 — anterior branch to the right ventricle.

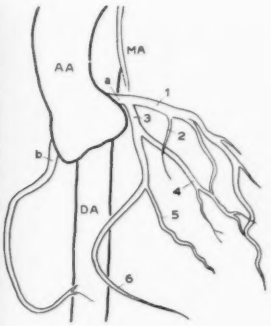
Fig. 1. Normal angiography of the coronary arteries in a boy 12 years old. Lateral projection.

only in selected cases permits contrast-filling of the coronary arteries and still more seldom outlines both the right and the left. In our monograph we state that 'if the technique used in performing the aortography be correct, filling of the coronary arteries is invariably obtained'. This has been confirmed in all our publications on the subject, both in living human subjects and in experimental conditions in dog.

From the cases examined with thoracic aortography at Roentgen Department I of Södersjukhuset, 96 were selected for this study because particularly complete filling had been achieved and the definition was so sharp as specifically to lend itself to a morphologic investigation. The patients' ages ranged from 7 to 69 years.

Post-mortem arteriographic studies on coronary alterations induced by age were performed by Rossi & Orlandini and Cella. Post-mortem arteriographic features of coronary sclerosis were particularly investigated by Schoenmackers & Vieten and Müller-Mohnssen. Coronary arteriography was successfully employed by Thal, Lester, Richards, and Murray in 18 patients with arteriosclerotic disease of the heart.





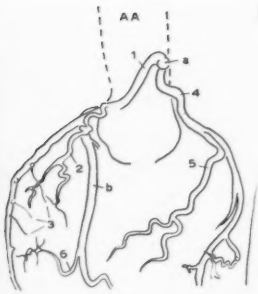
AA — ascending aorta, DA — descending aorta, MA — mammary artery, a — left coronary artery, 1— anterior interventricular branch, 2 — left conus branch, 3 — circumflex branch, 4 — branch to the obtuse margin, 5 — posterior branch to the left ventricle, 6 — posterior interventricular branch, b —right coronary artery.

Fig. 2. Normal coronary arteriography in a patient aged 28. A. p. view. Sinuosity along the anterior interventricular branch.

The results of my own investigations may be summarized as follows.

Up to 15 or 20 years of age (See Fig. 1), the coronary arteries present no sinuosity, their outlines are exceedingly sharp and smooth, the diameter gradually and uniformly tapers off from the center towards the periphery, and the contrast-filling always appears homogenous. As compared to the volume of the heart, the arteries appear well-developed and closely spaced.

From 20 to 40 years of age (See Fig. 2), the coronary arteries form obvious sinuosities, more particularly along the anterior interventricular

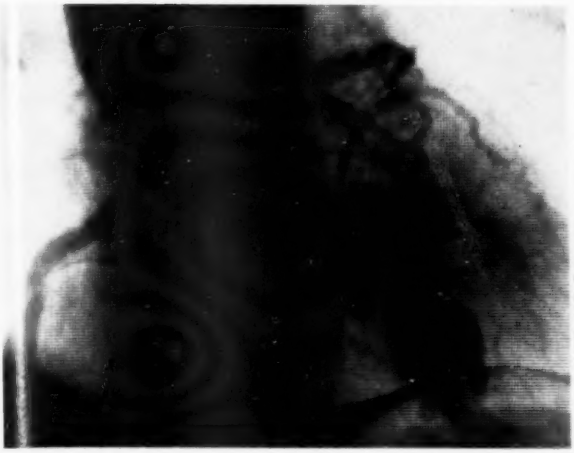


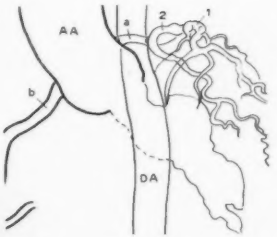
AA — ascending aorta, a — left coronary artery, 1 — anterior interventricular branch, with (2) left branch, 3 — septal branches, 4 — circumflex branch, 5 — branch to the obtuse margin, b — right coronary artery, 6 — branch to the acute margin.

Fig. 3. The coronary arteries in a patient aged 44. Lateral view. Small tortuosities along all the branches of the left coronary artery. The large coronary branches tend to a cylindrical shape.

branch, which is most clearly seen during ventricular systole. The arteries are still sharply and smoothly outlined, however, and the diameter has increased in proportion to the growth of the heart.

After the age of 40 (Fig. 3), the sinuosities of the coronary branches become generally more obvious and take on the appearance of small tortuosities, particularly along the anterior interventricular branch and during ventricular systole (although the feature is now clearly evident during ventricular diastole as well). The increase in diameter of the arteries is usually not proportional to the growth of the heart, although it should be noted that the arteries may seem less developed because they are spaced more widely apart. The coronary contours present a number of irregular spots, notably where a secondary ramification arises. The arterial lumen tends to become cylindrical in shape and the diameter appears almost constant from the proximal to the distal part of the vessel, instead of showing the normal slow decrease.





AA — ascending aorta, DA — descending aorta, a — left coronary artery, 1 — anterior interventricular branch, which is subdivided in three or more tortuous ramifications, 2 — circumflex branch, b — right coronary artery.

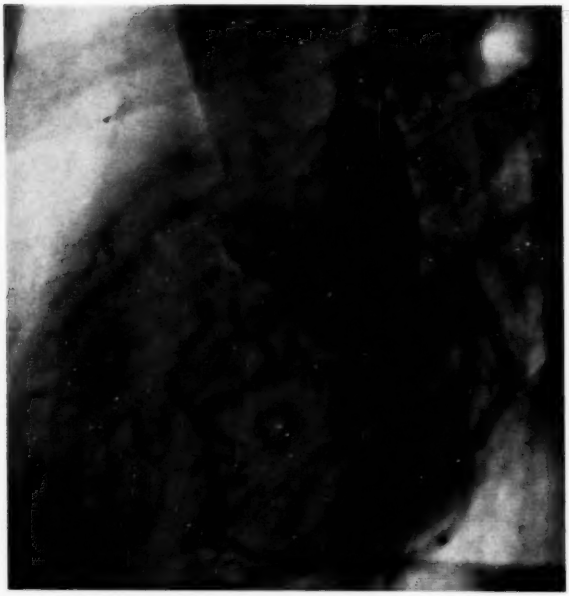
Fig. 4. Patient aged 69 with aneurysm of the aorta. High degree of tortuosity of the branches of the left coronary artery. The right coronary is cylindrical and rather dilated.

Very late in life (Fig. 4), or when certain pathologic conditions exist, the aforementioned changes become more accentuated and the picture of coronary sclerosis appears, with some typical arteriographic features that may briefly be summarized as follows.

1. Tortuosity (with a corresponding lengthening of the artery). Kinks and sharp bends are clearly defined along the larger central branches but even more evident in the smaller peripheral sections. These tortuosities do not vary during the heart cycle, but may become slightly emphasized in ventricular systole. They are most frequently observed in the anterior interventricular branch, and its secondary ramifications, and less likely to be found along the right coronary artery or the posterior interventricular branch; they are exceptional in the circumflex branch. In some cases all the branches of the coronary arteries present more or less marked tortuosities.

2. Irregularities in the diameter of the lumen. Rather than tapering off gradually and uniformly from the center to the periphery, the coronary branches acquire a cylindrical shape with sharply constricted sections distal to the points where the lesser ramifications arise.

3. Irregularity of outline. The vasal outline is bound to present several gaps, and a number of small filling defects are often detectable along the contours, probably caused by atheromatous areas protruding



AA — ascending aorta, a — left coronary artery, 1 — anterior interventricular branch with (2) left conus branch and (3) right branch, 4 — circumflex branch, b — right coronary artery, 5 — anterior branch to the right ventricle, 6 — branch to the acute margin, 7 — posterior part of the right coronary artery with marked irregularities of contours.

Fig. 5. Coarctation of the aorta. Sclerosis of the coronary arteries in a patient aged 32. High degree of tortuosity of the coronary branches. Lumen uneven, filling defects and interruptions of the contours along the right coronary artery (arrows).

within the lumen. Due to such anatomical conditions, the arterial walls may be vaguely outlined by the contrast medium.

My findings in the material of 96 cases now considered may in respect of changes be summarily divided into three groups termed: 'small tortuosities', 'major tortuosities', and 'generalized sclerotic features', the last mentioned group including such irregularities as filling defects along the contours. It is evident, as will appear from the Table below, that the changes referred to increase with age. The only case recorded in our youngest age group with 'small tortuosities' represents a patient who was 20 years old.

The signs of coronary sclerosis were most frequently found in patients suffering from coarctation of the aorta. 'Major tortuosities', or 'generalized sclerotic features' were found in 5 subjects, aged 20 to 25, and all of these had coarctation.

Fig. 6. Same case as in fig. 5. Film exposed two seconds later. The alterations described are constant. The tortuosities are now more evident in the small ramifications.

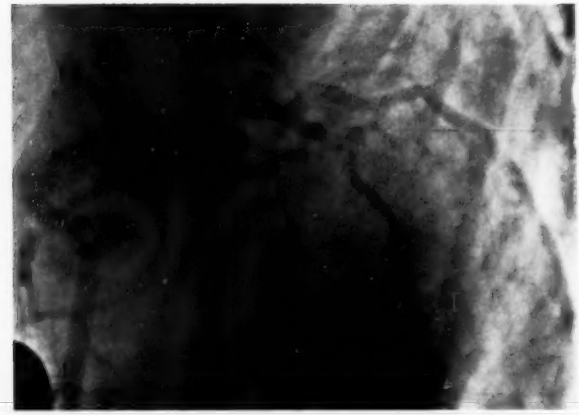
AA — ascending aorta, a — left coronary artery, 1 — anterior interventricular branch, with (2) left conus branch, 3 — left branch, 4 — circumflex branch, with obvious irregularity of the lumen at the origin, b — right coronary artery, with filling defects and interruption of contours (arrows), 5 — anterior branch to the right ventricle, 6 — posterior part of the right coronary artery. Possible anastomosis between right coronary artery and the circumflex branch of left coronary artery.

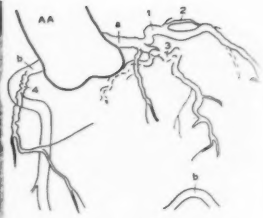
Coronary tortuosities are less frequently observed in acquired heart conditions with a greatly enlarged heart. on account of the fact that in such cases the coronary branches can be considerably stretched and the sinuosities may thus be smoothed out. The only clues to coronary sclerosis are then provided by the irregular outlines and the cylindrical appearance of the vessels.

Table 1

Arteriographic findings in a material of 96 cases

Age in years	up to 20	21—30	31—40	over 40
Normal	37	20	9	2
Small tortuosities	1	3	6	3
Major tortuosities	—	2	3	5
Generalized sclerotic features	—	—	1	4
Total	38	25	19	14





AA — ascending aorta, a — left coronary artery, 1 — anterior interventricular branch, 2 — left conus branch, 3 — circumflex branch, b — right coronary artery, 4 — right conus branch with highly irregular contours.

Fig. 7. Coarctation of the aorta. Sclerosis of the coronary arteries in a patient aged 34. Tortuosity and kinks of the coronary branches. Both right and left coronaries are rather enlarged and cylindrical in shape, contours irregular; contrast-filling of non-homogenous density.

Conclusions. The use of coronary arteriography may be of value in the study of coronary sclerosis for the following reasons.

I. In the initial stage of the condition, when obstructions are still rare and very slight, there will be no electrocardiographic changes or any clinical symptoms or signs to indicate the extent of sclerotic damage. At this stage therefore, arteriography may be the only method by which vascular changes can be demonstrated.

II. At a later stage, arteriosclerotic alterations may be indicated by electrocardiographic findings, but little information can be obtained from the latter as to where the alterations are located or how marked they are. Arteriography readily provides such information.

III. At a still later stage, when clinical and electrocardiographic signs are most evident (angina, myocardial infarction), the following information may be provided by arteriography: 1) exact location and extent of the infarction, 2) condition of the other coronary branches, notably as regards sclerotic damage, 3) evidence of a collateral circulation, if any, and 4) detection of possible coronary obstructions in such myocardial areas as are not responsive to electrocardiography. All the above data might be of the greatest value from the point of view of possible surgical treatment.

SUMMARY

Out of 274 cases in which the coronary arteries were demonstrated in living subjects, 96, in which complete filling was obtained, were selected as being particularly suitable for a profitable morphologic investigation. The age of these patients ranged from 7 to 69 years. Alterations in the coronary arteries at different ages and the most significant arteriographic findings in coronary sclerosis are described. The usefulness of arteriography in the study of the condition is emphasized and the possible surgical value of the data obtained is pointed out.

ZUSAMMENFASSUNG

Aus einer Reihe von 274 Fällen, in denen die Koronararterien am Lebenden dargestellt werden konnten, wurden 96 mit einer völligen Ausfüllung der Arterien als besonders geeignet für eine ergiebige morphologische Untersuchung ausgewählt. Das Alter dieser Patienten lag zwischen 7 und 69 Jahren. Veränderungen der Koronararterien in verschiedenen Lebensaltern und die bedeutendsten arteriographischen Befunde bei der Koronarsklerose werden beschrieben. Der Wert der Arteriographie für das Studium dieser Erkrankung wird betont und die Bedeutung der erhobenen Befunde für eventuelle chirurgische Eingriffe wird hervorgehoben.

RÉSUMÉ

Sur 274 cas où les artères coronaires avaient été mises en évidence chez des sujets vivants, l'auteur en a retenu comme particulièrement utiles pour une étude morphologique 96 cas où l'opacification complète avait été obtenue. L'âge de ces sujets allait de 7 à 69 ans. L'auteur décrit les altérations des artères coronaires aux différents âges et les signes artériographiques les plus importants dans la sclérose coronarienne. Il souligne l'utilité de l'artériographie pour l'étude de cette affection et indique l'intérêt chirurgical possible des renseignements obtenus.

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FROM ROENTGEN DEPARTMENT I (DIRECTOR: DOCENT GUNNAR JÖNSSON), SÖDERSJUKHUSET, STOCKHOLM, SWEDEN

ELECTROKYMOGRAPHIC STUDIES IN AORTIC STENOSIS

by

Olle Marions and *Per Ödman*

The possibility of surgical treatment of aortic stenosis has increased the demands on the diagnostic analysis. Methods which directly demonstrate the hemodynamic and anatomical changes have therefore been developed, e. g. angiographic procedures of various kinds, and intravascular and intracardiac pressure and pulse recordings. These methods are, however, hazardous, often complicated and, for that reason, suitable only for cases selected with a view to operation.

Bloodless and therefore safer pulse recording methods, such as electrokymography, have also been tested. Several authors (ENGSTRÖM et coll., KJELLBERG et coll., REINHOLD et coll., HEYER et coll., HEYER & BOONE, DACK & PALEY, DEUTSCH et coll., HAUBRICH, MAGISTRETTI et coll.) have shown that in cases of aortic stenosis there may be distinct changes in the aortic electrokymogram. The gradient of the curve during the systolic upstroke may be diminished, sometimes with sharp angulation, i. e. anacrotic notch, followed by a less steep limb (Fig. 3). The transition between the rapid and slow ejection phases, corresponding to the upper part of the curve, is sometimes rounded, at least in the ascending aorta electrokymogram (KJELLBERG et coll.). Normally, there is on the aortic

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ejection curve a peak or an inflection followed by a saddle-shaped segment (KJELLBERG et coll.). The incisura corresponding to aortic valve closure, and the subsequent dicrotic upswing are often indistinct or absent (Fig. 3). Finally, the aortic curve during diastole may be convex upwards (KJELLBERG et coll.). In most accounts these criteria appear to be based on isolated cases, and sometimes it is not stated where on the thoracic aorta the pathologic curves were recorded, although certain differences in shape as well as in chronology have been shown between electrokymograms from different segments of the aorta (KJELLBERG et coll.). The publications therefore provide no exact conception of the value of electrokymography in the diagnosis of aortic stenosis. The exception is KJELLBERG et coll.'s work comprising electrokymographic studies in 16 children with congenital valvular or subvalvular aortic stenosis. These cases are thoroughly investigated. In two of them, for instance, changes in the valve apparatus have been demonstrated by angiocardiography. This material, however, represents special types of aortic stenosis from a certain hemodynamically characteristic age-group.

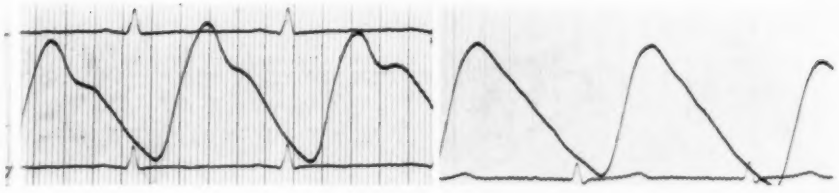
The usefulness and limitations of electrokymography in aortic stenosis have thus hardly been evaluated. We have therefore examined the electrokymograms, paying special attention to the appearance and chronology of the aortic curve from different segments of the aorta in cases of aortic stenosis where the diagnosis has been made with reliable methods. These have been compared with analogous curves from other acquired and congenital valvular lesions from a normal material and from some other heart and circulatory diseases.

The electrokymographic examinations were carried out with the patient sitting, or, in some instances, in the supine or the prone position, according to principles described earlier by one of the authors (ÖDMAN). The apparatus described by ANDERSSON was used. Electrocardiogram (ECG), lead II, served as reference.

The patients were clinically examined with ECG, phonocardiography, and conventional roentgenography, and to a large extent further analysed by angiocardiography and intracardiac pressure and pulse recordings.

The material has been divided in the following way:

I. *Aortic stenosis group*, comprising 29 cases between the ages of 13 to 78 years, all with regular rhythm. Five of these were investigated electrokymographically twice or more; these were considered to have predominant aortic stenosis. In 15 cases the diagnosis had been made by thoracic aortography or angiocardiography. Typical changes in the valves together with narrowing of the aortic ostium (PORJÉ et coll., ARVIDSSON, ÖDMAN & PHILIPSSON) were present in all these cases. Five of them presented a dome-shaped deformation of the valves during



a b

Fig. 1. Normal subject. Aortic arch electrokymograms: a) with distinct incisura and dicrotic wave, b) without incisura.

stole, which characterizes the congenital form of valvular aortic stenosis (Kjellberg et coll., Ödman & Philipsson). The other cases in the group, which were not examined with contrast medium, all had demonstrable calcification of the aortic valves, this also being a definite indication of aortic stenosis (Parkinson, De Fazio & Marsico).

II. *Aortic insufficiency group*, comprising 10 cases between the ages of 25 to 79 years with regular rhythm. These were considered to have predominant aortic insufficiency. The diagnosis was based on clinical findings such as blood pressure, auscultation etc. Three cases had also been examined by thoracic aortography, at which the contrast medium regurgitated to the left ventricle, thus giving a direct demonstration of the insufficiency of the valve apparatus (Castellanos & Garcia and others).

III. *Mitral disease group*, comprising 15 cases between the ages of 25 to 46 years. Of these, 10 had predominant mitral stenosis, 2 predominant mitral insufficiency, and 3 both stenosis and insufficiency. All except one, had regular rhythm. The diagnosis was based on angiocardiographic studies with the main emphasis on the cyclic volume variation of the left atrium. These cases are all described and thoroughly discussed in Arvidsson's thesis. The aortic valves and the left ventricle could in all cases be appraised at the angiocardiographic examination. There was no basis for suspecting aortic stenosis in any of the cases.

IV. *Combined group*, comprising 16 cases between the ages of 26 to 46 years, all having both mitral and aortic valvular lesions. All cases had regular rhythm and were examined angiocardiographically according to Arvidsson's principles; in two cases thoracic aortography also was carried out. All cases were considered to have aortic stenosis of varying degree, and one case had a clinically significant concomitant aortic insufficiency.

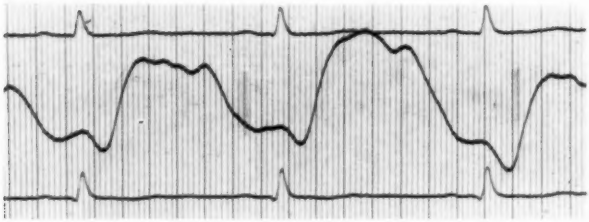


Fig. 2. Normal subject. A rounded transition between rapid and slow ejection.

V. *Mixed group*, comprising two cases with hypertension, 3 with cardiac infarct, 4 with pericarditis, 4 with patent ductus arteriosus, and 6 cases with atrial or ventricular septal defect.

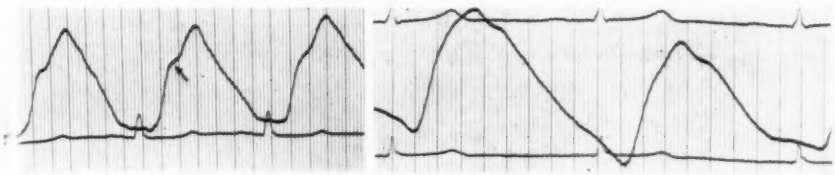
Finally, electrokymograms of 25 cases from a psychiatric material between the ages of 17 to 55 years have been used as controls. These were clinically judged as having normal hearts, and we have therefore assumed that their electrokymograms were normal.

Curves from the cardiac chambers as well as the thoracic aorta were recorded. In aortic stenosis, however, distinct pathologic changes in electrokymograms from the cardiac chambers occurred only in exceptional instances. It is sufficient here to cite a prolonged atrial contraction descent in the left atrial curve, an unspecific finding showing the impeded emptying of the atrium (LUISADA, ÖDMAN).

The aortic electrokymograms therefore attracted the main interest and only these will be discussed below.

Specific variations in shape of the electrokymographic curves, similar to those mentioned in the introduction, could often be observed in the aortic stenosis group. However, diagnostic importance could only rarely be attached to these for the following reasons.

Recordings from the same segment of the thoracic aorta varied both from patient to patient, and on different occasions in the same patient. This applied particularly to the electrokymograms of the ascending aorta, as BRANDFONBRENER & EISENBERG have pointed out. Positional changes as well as influence from the hilum vessels seem to have a completely different effect on the appearance of these curves recorded in adults from those recorded in children. According to KJELLBERG et coll. the ascending aorta curves of the latter are well suited for diagnostic judgement. Phenomena previously regarded as characteristic of aortic stenosis appeared in normal subjects, and in other valvular lesions. Moreover, some of these phenomena were relatively rare in the aortic stenosis group.



a b

Fig. 3. Predominant aortic stenosis. a) Ascending aorta curve. Distinct anacrotic notch. b) Aortic arch curve. Anacrotism indicated only by change in gradient.

The anacrotic notch was present in only two cases of aortic stenosis, and in the same number of cases in the combined group. Distinct anacrotism occurred mostly in the ascending aorta curves. In the aortic arch electrokymograms this phenomenon appeared as a more or less distinct change in gradient (Fig. 3).

Incisura and subsequent dicrotic wave were absent or very indistinct in the curves from the aortic arch in 24 cases from the aortic stenosis group. In at least 8 of the normal subjects, however, a clear incisura and dicrotism were likewise absent (Fig. 1b). BRANDFONBRENER & EISENBERG published similar observations. In the mitral disease group this finding was made in 8 cases and in the aortic insufficiency group in 9 cases out of 10. These facts are the more remarkable as, according to ENGSTRÖM et coll., HEYER et coll., WENGER and HAUBRICH, the ab-

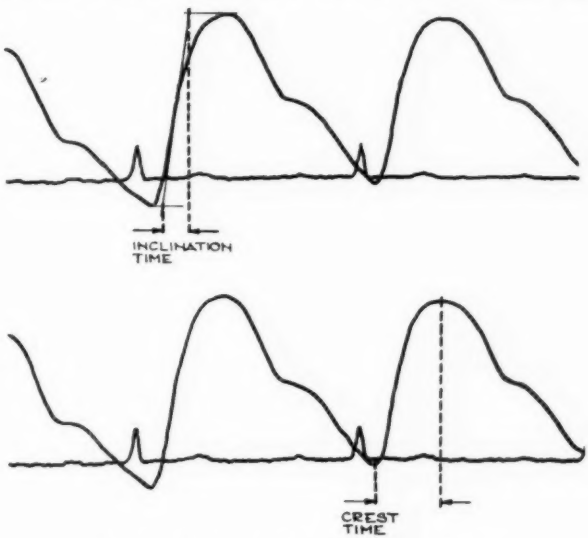


Fig. 4. Definition of inclination and crest times.

Table

Values from aortic arch electrokymograms in mixed group

	Inclination time	Crest time	Passage time	Interval between highest point of systolic upstroke and incisura
	sec	sec	sec	
Hypertension	0.08—0.09	0.12—0.14	0.14—0.19	0.09—0.10
Cardiac infarct	0.11—0.13	0.18—0.21	0.13—0.19	0.08
Pericarditis	0.09—0.13	0.15—0.22	0.12—0.16	0.09—0.10
Patent ductus arteriosus	0.09—0.15	0.18—0.24	0.13—0.18	0.06—0.09
Atrial or ventricular septal defect	0.08—0.11	0.16—0.19	0.10—0.15	0.08—0.14

sence of dicrotism and incisura characterizes the aortic electrokymogram of aortic insufficiency.

A more or less rounded transition between the systolic upstroke and the descending limb was observed in the ascending aorta electrokymograms of at least 8 normal subjects (Fig. 2). In the group of aortic stenosis this could be seen in 17 cases and in the group of mitral valvular lesions in 7 cases. It was, incidentally, present in all five cases of mitral insufficiency.

No typical features in the shape of the aortic curves during diastole could be demonstrated in the aortic stenosis group. The upward convexity pointed out by KJELLBERG et coll. occurred in only 2 cases.

In order objectively to demonstrate the various changes in the aortic curves, certain measurements were made. The electrokymograms of the ascending aorta often gave unreliable results, and therefore only the measurements from the aortic arch will be discussed here. In cases with irregular rhythm the results from different heart cycles in the same electrokymographic recording could vary. Such cases have therefore been excluded. These, however, do not affect the discussion concerning the aortic stenosis, as all these cases had regular rhythm.

In order to obtain a measurement of the rapidity of ascent of the systolic upstroke the inclination (LUND) and crest times (YAMAGUCHI, DILLON & HERTZMAN) were defined (Fig. 4), as with measurements used in other bloodless pulse recording methods. If there was an anacrotism with different gradients above and below the notch, the inclination time was decided on the lower segment of the systolic upstroke.

One cannot exclude the possibility that the inclination and crest times are influenced by the degree of enlargement in the electrokymographic recording. Practical tests made under identical conditions but with varying enlargement show, however, that one can ignore this source of error (Fig. 5). Further, it should be pointed out that the degree

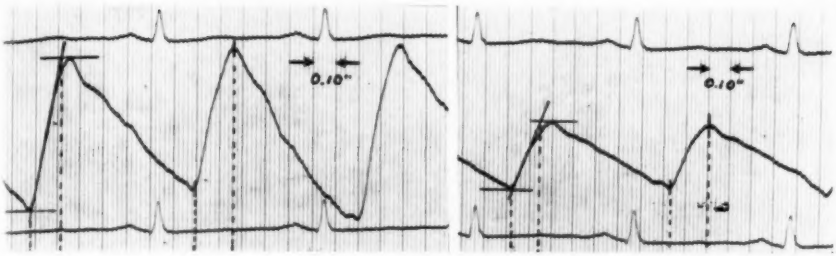


Fig. 5. Curves, in different enlargements, of the aortic arch. Inclination and crest times are the same in both cases.

of enlargement within different segments of the slit of the phototube varies (cf. BRANDFONBRENER & EISENBERG). This may possibly have an influence upon individual recordings, but one can hardly attach any importance to it in the comparison of results from different diagnostic groups.

If one compares the inclination and crest times in the different groups, one finds the longest duration in the aortic stenosis group (Diagrams 1 and 2, and the Table). Second comes the combined group, i. e. cases which have also aortic stenosis although not predominantly. There are also some high values in the aortic insufficiency group. An extra long inclination time seems above all to characterize aortic stenosis, in that approximately two-thirds of these cases had higher values than the maximum in the controls. The cases of aortic stenosis that fall within this limit belong almost exclusively to the higher age-group; seven of them were older than 55 years. The prolongation of the inclination and crest times is not, as far as we could find, directly correlated to the severity of the aortic stenosis. We have observed cases showing shorter as well as longer inclination and crest times, after the onset of stasis.

Further, the passage time was determined in all cases, i. e. the interval between the Q-wave in ECG and the beginning of the systolic upstroke. This phenomenon is interesting in this connection as it shows at what stage in the heart cycle the aorta begins to widen. Approximately the same value was recorded in all groups. But it should be pointed out that in the aortic insufficiency group unusually low passage times were recorded on the ascending aorta curves. On the other hand, no such deviation appeared in the aortic arch curves. (See Diagram 3 and Table.)

Finally, the interval between the highest point of the systolic upstroke, and the incisura corresponding to the closure of the valves was determined. Our intention was to elucidate the relation between the end

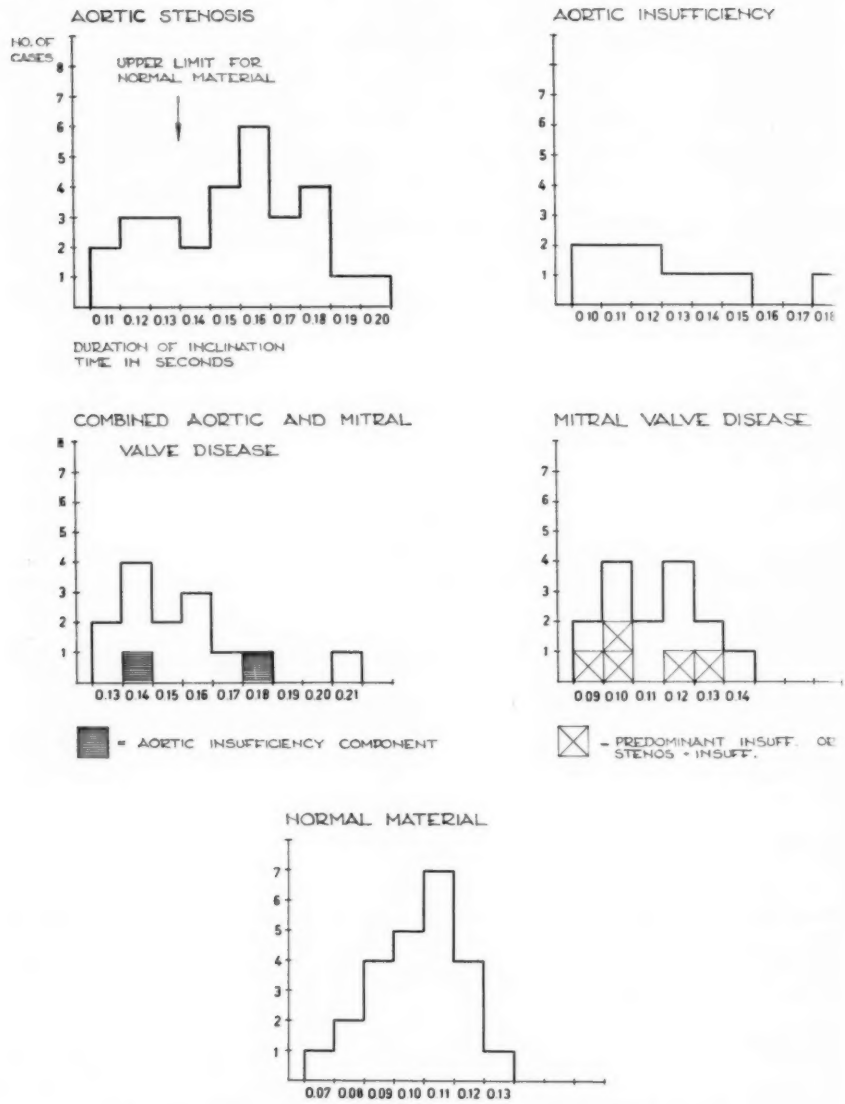

AORTIC STENOSIS
NO. OF CASES
UPPER LIMIT FOR NORMAL MATERIAL
0.11 0.12 0.13 0.14 0.15 0.16 0.17 0.18 0.19 0.20
DURATION OF INCLINATION TIME IN SECONDS
AORTIC INSUFFICIENCY
0.10 0.11 0.12 0.13 0.14 0.15 0.16 0.17
COMBINED AORTIC AND MITRAL VALVE DISEASE
0.13 0.14 0.15 0.16 0.17 0.18 0.19 0.20 0.21
= AORTIC INSUFFICIENCY COMPONENT
MITRAL VALVE DISEASE
0.09 0.10 0.11 0.12 0.13 0.14
= PREDOMINANT INSUFF. OR STENOS + INSUFF.
NORMAL MATERIAL
0.07 0.08 0.09 0.10 0.11 0.12 0.13

Diagram 1. Inclination time recorded on aortic arch electrokymograms.

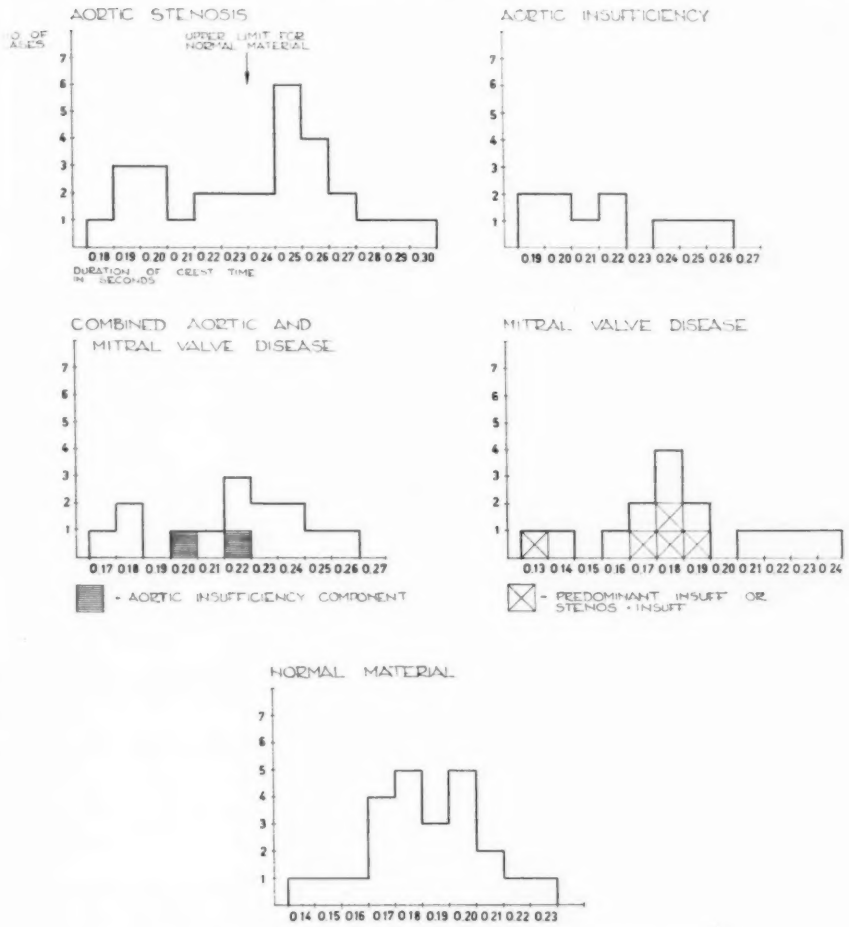

AORTIC STENOSIS
UPPER LIMIT FOR NORMAL MATERIAL
0.18 0.19 0.20 0.21 0.22 0.23 0.24 0.25 0.26 0.27 0.28 0.29 0.30
DURATION OF CREST TIME IN SECONDS
AORTIC INSUFFICIENCY
0.19 0.20 0.21 0.22 0.23 0.24 0.25 0.26 0.27
COMBINED AORTIC AND MITRAL VALVE DISEASE
0.17 0.18 0.19 0.20 0.21 0.22 0.23 0.24 0.25 0.26 0.27
- AORTIC INSUFFICIENCY COMPONENT
MITRAL VALVE DISEASE
0.13 0.14 0.15 0.16 0.17 0.18 0.19 0.20 0.21 0.22 0.23 0.24
- PREDOMINANT INSUFF OR STENOS - INSUFF
NORMAL MATERIAL
0.14 0.15 0.16 0.17 0.18 0.19 0.20 0.21 0.22 0.23

Diagram 2. Crest time recorded on aortic arch electrokymograms.

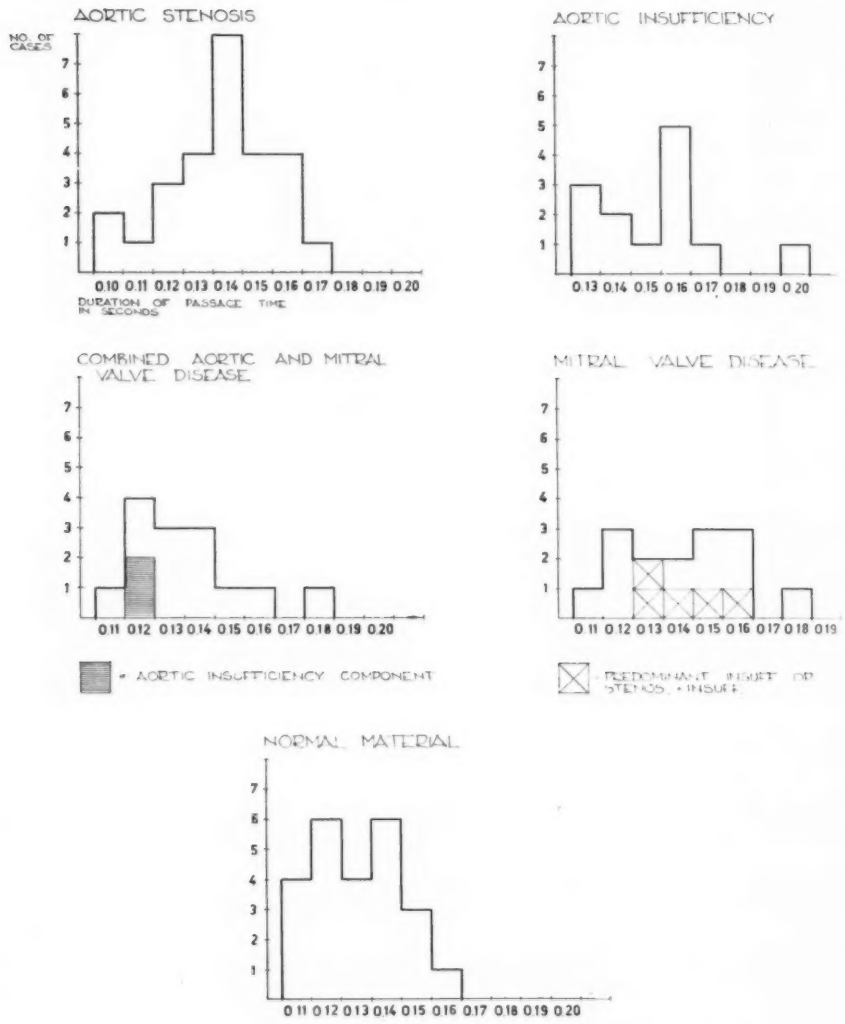


Diagram 3. Passage time from aortic arch electrokymogram.

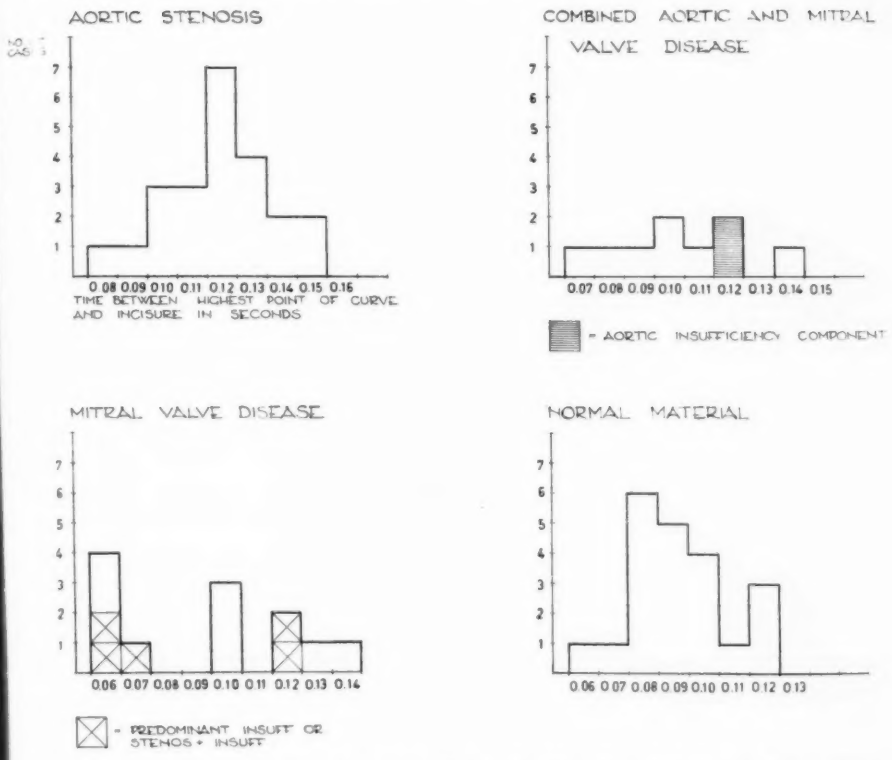

AORTIC STENOSIS
0.08 0.09 0.10 0.11 0.12 0.13 0.14 0.15 0.16
TIME BETWEEN HIGHEST POINT OF CURVE AND INCISURE IN SECONDS
COMBINED AORTIC AND MITRAL VALVE DISEASE
0.07 0.08 0.09 0.10 0.11 0.12 0.13 0.14 0.15
= AORTIC INSUFFICIENCY COMPONENT
MITRAL VALVE DISEASE
0.06 0.07 0.08 0.09 0.10 0.11 0.12 0.13 0.14
= PREDOMINANT INSUFF OR STENOS + INSUFF
NORMAL MATERIAL
0.06 0.07 0.08 0.09 0.10 0.11 0.12 0.13

Diagram 4. Interval between highest point of systolic upstroke and incisura in an aortic arch electrokymogram. (No such determination could be made in the aortic insufficiency group.)

of systole and the two ejection phases (cf. KJELLBERG et coll.). Among the cases of aortic stenosis we often found relatively high values, as also among the cases of mitral stenosis (Diagram 4). This prolongation does not therefore appear to be a phenomenon specific to aortic stenosis. The diagnostic value of this phenomenon is further reduced by the fact that in some of the cases of aortic stenosis the incisura is absent. This was so also in some of the other diagnostic groups.

Discussion

Some workers have previously maintained that changes in the shape of the aortic curve constitute comparatively uncertain criteria of aortic stenosis, and that the individual variability makes judgment more difficult

(ENGSTRÖM et coll., DACK & PALEY, HEYER et coll., MAGISTRETTI et coll., and others). This is confirmed by our investigations (Figs. 1b and 2). Even anacrotism on the systolic upstroke appears to be an uncertain and rare indication. It may be pointed out in this connection, that although anacrotism did not appear in our controls, BRANDFONBRENER & EISENBERG have observed this phenomenon amongst healthy subjects. The inclination and crest times are the most dependable elements in the electrokymographic diagnosis of aortic stenosis. In certain doubtful cases these have even had decisive significance. It has earlier been maintained (KJELLBERG et coll., and others) that the reduced rapidity of ascent of the systolic upstroke is a sign of the prolonged emptying of the left ventricle and of the abnormal function of the aortic orifice. In our investigations, however, certain age-conditioned differences as to the inclination and crest times appear, which indicate that other factors can also have an effect. With regard to the age correlation, one has reason to suppose that the elasticity of the walls of the aorta, peripheral resistance etc., also have an influence. We have been unable clearly to establish in our adult cases the connection between reduction of ascent of the systolic upstroke and the severity of the aortic stenosis that KJELLBERG et coll. seem to have found in children. It seems probable that the stroke volume has an effect on the inclination and crest times in that the length of the ascent becomes relatively shortened when the left ventricle fails, with the result that these values are lessened in a corresponding degree. Certain observations in connection with pressure recording over the aortic ostium indicate a parallel phenomenon — when the ventricle fails the pressure gradient usually lessens (HANSSON & KARNELL, personal communication).

It is of interest from a differential-diagnostic point of view to know that even aortic insufficiency can have long inclination and crest times. The two cases with the longest inclination time in the insufficiency group have been carefully examined clinically, and thoracic aortography has been carried out, without it being possible to show any obvious stenotic component.

This observation is significant, as the clinical diagnosis can also prove difficult when one is faced with the alternatives of aortic stenosis or insufficiency. On the other hand, fairly reliable electrokymographic differences exist: aortic insufficiency often shows a short passage time on the ascending aorta curves and/or indistinct gradual transition between the isometric contraction and the systolic upstroke. Furthermore, dicrotism and incisura are much more often absent in cases of aortic insufficiency than in stenosis. The insufficiency curve, which normally tends to rise very steeply with a distinct peak, falls rapidly in diastole, frequently with a concave course.

SUMMARY

Electrokymographic examinations have been carried out in 29 cases of predominant ortic stenosis and the results compared with normal electrokymograms and with those f other valvular lesions. Aortic stenosis is characterized by a decreased gradient in the ystolic upstroke in the electrokymogram of the aortic arch. By determining the in- lination and crest times it has been possible to demonstrate this phenomenon objec- ively. A prolonged inclination and crest time appears to be a reliable criterion of aortic tenosis.

ZUSAMMENFASSUNG

Elektrokymographische Untersuchungen sind in 29 Fällen mit prädominanter Aortenstenose durchgeführt worden. Die Ergebnisse wurden mit normalen Elektrokymogrammen und mit solchen anderer Klappenerkrankungen verglichen. Die Aortenstenose wird durch einen niedrigen Gradienten im systolischen Anstieg des Elektrokymogrammes des Aortabogen charakterisiert. Durch Bestimmung der Inklination und der Anstiegdauer ist es möglich geworden, dieses Phänomen objektiv zu demonstrieren. Eine verlängerte Inklination und Anstiegdauer scheint ein zuverlässiges Kriterium der Aortenstenose zu sein.

RÉSUMÉ

Les auteurs ont fait des examens électrokymographiques dans 29 cas de sténose aortique prédominante et ont comparé les résultats avec des électrokymogrammes normaux et avec ceux d'autres lésions valvulaires. La sténose aortique se caractérise par une diminution du gradient du crochet systolique de l'électrokymogramme de l'arc aortique. La mesure de la durée de la pente et de la crête a permis de mettre ce phénomène en évidence de façon objective. L'allongement de la durée de pente et de crête semble être un critère fidèle de sténose aortique.

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FILLING AND MOULDING OF THE CEREBRAL FLUID AND VASCULAR SYSTEMS OF THE BRAIN BY MEANS OF A NEW PLASTIC

by

Hans Eckerbom

Great collections of anatomical models were amassed at medical schools and in Aisklepion temples during the period of Hellenic culture. These 'votive tablets' were originally intended as objects of sacrifice but they must certainly have been of considerable importance for teaching purposes. This method of teaching and memorizing remains valuable to this day especially in the case of the more complicated anatomical structures. Every roentgenologist knows the difficulty of retaining a clear picture of the topography of the vessels and ducts of the human body and, although a three-dimensional impression may be gained by the comparison of roentgen views obtained in various planes, the interpretation is often rendered much more easy by the study of a topographic model.

Up to the middle of the 17th century stuffing and fixation in alcohol or formaldehyde were the only means available for preserving the whole or part of an animal, closer knowledge of the anatomy being obtained by dissection. The impressions of the findings were recorded in the form of sketches, mostly somewhat primitive, although exceptionally a few great artists were able to raise the method to superb heights (Dürer, Leonardo da Vinci).

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A physician from Leyden, one Johannes Swammerdam, in about 1650 was the first to use melted wax for the filling of vessels and ducts. The corrosion of tissues was at this time unknown and the material had to be dissected out with the utmost care. Friedrich Ruysch, also of the Netherlands, is said to have introduced the method of corrosion at the end of the 17th century. He utilized insect larvae and ordinary putrefaction for the destruction of the soft tissues, the wax mould being left in situ. Mineral acids were later employed for the same purpose, first by Nathanael Lieberkühn of Berlin in 1748.

Alloys of tin, lead, and bismuth were introduced towards the end of the 17th century and produced less fragile models. Some of these alloys have a very low melting point, e. g. Wood's metal, which melts at 65° to 70° C. This method enabled Gottfried Bidloo to make beautiful casts of the bronchial tree in 1685, and many other models have later been obtained in the same way. Gustaf Retzius of Stockholm (KEY & RETZIUS 1875) made a cast of the ventricular system of the brain at the end of the 19th century, a model which is of a particular neuroradiologic interest: he was not able, however, to produce a complete cast at one time but had to build up his model from several sections. HYRTL of Vienna should not be omitted from the names of the pioneers of anatomical mouldings; his models were mostly made with natural resins; his great work 'Die Korrosionsanatomie' with its excellent illustrations was published in 1873. Shellac and gelatine were introduced towards the end of the 19th century. These, and the earlier mentioned wax, belong chemically to the group of organic plastics derivatives. Later, derivatives of nitrocellulose were brought into use; thus celloidin was introduced by Schiefferdecker in 1882 and celluloid by Storch in 1899.

Various kinds of rubber solutions, such as neoprene and castolite, became available in about 1930. These, like the abovementioned natural resins, belong to the group of organic plastics. In 1947 HJORTSJÖ (BJÖRCK, BLOMSTRAND, HJORTSJÖ & LÖFGREN 1949) used colloidin and neoprene for studies of the topography of the liver.

The use of synthetic plastics was begun in 1935 with the introduction of vinylite as a medium for injection, and acrylic plastics came into use in 1948. Both of these belong to the so-called low-molecular polymerization plastics. HJORTSJÖ and his collaborators have been the pioneers in Sweden in this field and in 1949 they synthetized a vinylite-acrylic plastic which they called 'Corroplast Lund'. This compound was rendered roentgenopaque by the addition of 10 % to 20 % of mercury sulfide. In 1952 these Swedish workers produced a new polyisocyanate plastic, called polyurethan, which is also a polymerization product. Such compositions often produce quite good moulds although not even the best of them can be classed as ideal.

Plastics of animal origin such as animal wax, shellac, and gelatine, as well as mixtures of these, must be preheated, which is a great disadvantage particularly as the organ to be filled must also be warmed. Furthermore, there is a tendency for the media to solidify before they reach the finer arborizations. Some of the preparations produce very fragile casts, especially if colouring matter or barium sulphate is added. Rubber solutions are quite unsuitable because of the complicated technique needed and the slowness of the vulcanization process. Polymerization plastics constitute a great improvement, but the setting time of these materials is relatively long; it may extend to 24 hours in the case of the larger casts. Moreover, such plastics possess a marked tendency to shrink; the shrinkage may amount to 15 and 21 volume-percent for vinylites and acrylic plastics, respectively.

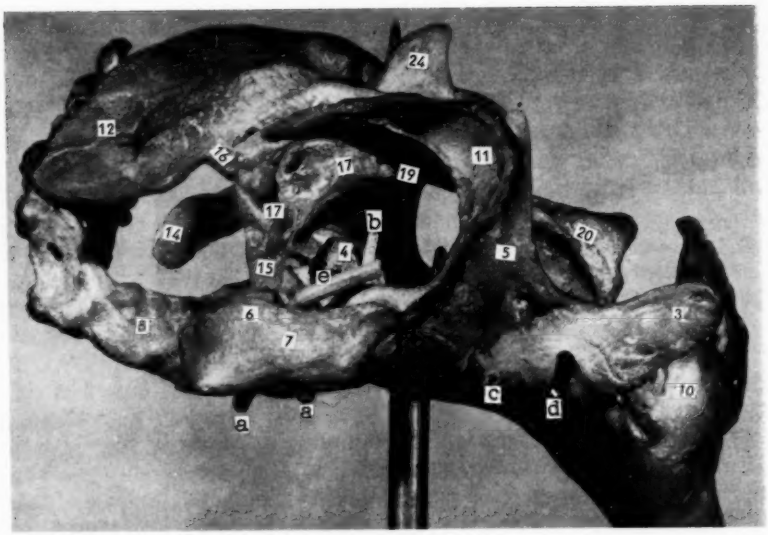
Polyurethan is superior to the earlier preparations but still has its disadvantages. The shrinking tendency is low, being only 8 volume-percent, but the setting time is long, reaching several hours. The important disadvantage, however, is the fact that the isocyanate group reacts with water to form carbon dioxide with the consequent production of minute bubbles of gas.

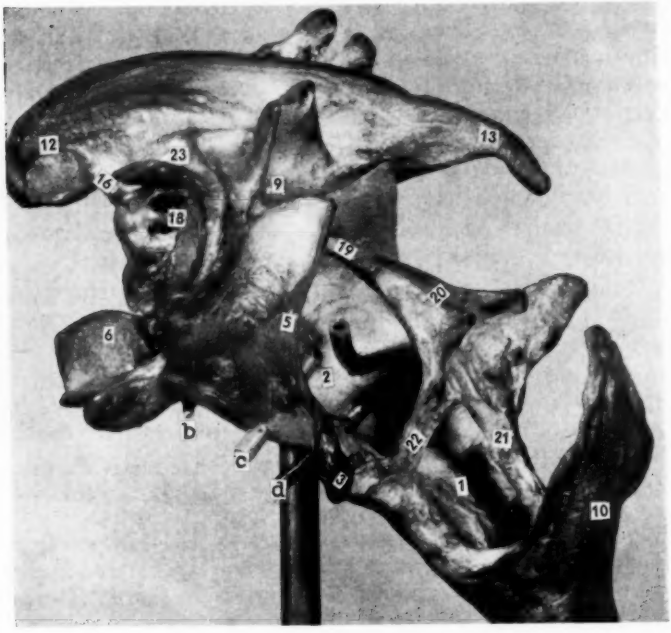
Progresses in industrial chemistry has brought about new high molecular unsaturated polyester resins which can be polymerized at room temperature after the addition of a catalyzer and an accelerator. The introduction of these preparations has constituted a most important progress in anatomical moulding. A material of this kind, Soredur, is manufactured in Sweden by Svenska Oljeslageri AB, Gothenburg. Markon resins, made by Scott Bader & Co in London, are also very suitable. Soredur has been at my disposal since 1956.

The demands that an ideal casting preparation should meet are the following:

1. The tendency to contract must be uniform and as low as possible.
2. Filling of both large and minute cavities must be possible.
3. Corrosives must not affect the cast.
4. The technique must be simple, quick, and applicable at room temperature.
5. The cast must be durable and firm.
6. The setting time and degree of hardness must be variable.
7. It must be possible to colour and render the cast roentgen-opaque.

Soredur, as received, is a yellowish, more or less viscous fluid, which can be hardened either at room temperature or higher. Hardening is attained by means of a peroxide catalyzer paste, called CHF, and a solution of cobalt naphtenate as an accelerator; the latter contains 6 % of cobalt. The process of hardening is by polymerization and no volatile





Bronze mould of the ventricular and cerebral fluid systems (key to letters and numbers, see opposite page).

l y-products are formed. The hardened object is quite homogenous and (f a faint lilac-colour.

The catalyzer must be thoroughly blended with the Soredur, the r ixture being stable for about 12 hours at room temperature. Immediately l efore using the composition the accelerator is gently stirred in; any l ubbles of air will disappear if the mixture is allowed to stand for a few r inutes. The shrinking of the hardened cast varies between 5 and 8 v olume-per cent.

Soredur is sold in various grades of viscosity. The types H_{20} and H_{30} have a viscosity o 750 and 1 100 centipoise, respectively. The viscosity can be further varied by adding st rene (a derivative of vinylbenzene), and by control of the temperature, as shown in T ble 1.

Table 1

Temperature	Styrene, %	Viscosity in centipoise
20° C	0	750
20° C	5	360
20° C	10	220
17° C	—	950
20° C	—	750
23° C	—	580

The addition of styrene and an increased temperature thus diminish the viscosity.

The 'setting time' is the time which elapses from the moment the hardener is added till the fluid congeals. It can be varied by the factors shown in Table 2.

Table 2

Catalyzer, %	Accelerator, %	Setting time, min
1	1.0	330
3	1.0	15
5	1.0	9
4	0.2	45
4	0.6	15
4	1.0	11

Key to the bronze mould, seen obliquely from front and from below (upper), and obliquely from behind and from above (lower view).

1. Medullary cistern
2. Pontine cistern
3. Cerebello-pontine cistern
4. Intercrural cistern
5. Crural cistern
6. Cistern of the lamina terminalis
7. Chiasmatic cistern
8. Cistern of fossa Sylvii
9. Quadrigeminal cistern
10. Cerebello-medullary cistern
11. Ambient cistern
12. Anterior horn of lateral ventricle
13. Posterior horn of lateral ventricle
14. Temporal horn of lateral ventricle
15. Optic and infundibulum recess
16. Foramen of Monro
17. Third ventricle
18. Massa intermedia
19. Aqueduct of Sylvius
20. Fourth ventricle
21. Foramen of Magendie
22. Foramen of Luschka
23. Cistern above the third ventricle
24. Cistern of corpus callosum (dorsal part)

a — Optic nerve
b — Oculomotor nerve
c — Trigeminal nerve
d — Auditory nerve
e — Mamillary bodies

A reduction in the setting time is thus obtained by increasing the amount of catalyze or accelerator.

Soredur may be obtained both 'hard' and 'soft'; types H_{20} and H_{30} are both hard an type M_{10} is soft; in objects which are to be examined only microscopically the soft ty should be used, as the hard type will tear the surrounding tissues when cut. Soredu possesses good chemical non-affinity. I have used 70 % sulphuric acid for tissue corrosio and as far as I have been able to judge no change in the cast has taken place. Soredur ma be tinted as desired by adding suitable colouring matter. This is of importance as it rende the simultaneous filling of different structures possible. If the amount of pigment exceed 1 to 2 % it will change the setting time, but in most cases a percentage of 0.1 is qui sufficient. Soredur may also be rendered roentgen-opaque by adding contrast material ; I have used a lead derivate to obtain as high an absorption as possible.

Soredur has proved to be an excellent preparation for casting anato ical structures, superior to any material used before, and approachi the ideal of an injection medium. I have used the preparation to mak casts of the vessels and the cerebral fluid system of the human brain. For anatomical purposes the results are best in well conserved cadavers of young subjects.

Only specimens in which the dura mater has remained intact after the removal of the calvarium can be used. The cerebral fluid system must be effectively drained and as much of the fluid as possible evacuated. This has been carried out by means of trocars in the great cistern, in the intercrural cistern, and in both the posterior cornuae. The filling with generally about 300 ml of fluid plastic material has also been made through these trocars. As the moist walls of the system and any remaining fluid act as inhibitors to the polymerization, it is of utmost importance to make the injection at the correct time to reduce this effect. Experience has shown that the injection should commence 3 to 4 minutes after the addition of the accelerator. The plastic-filled brain must then not be excised until 1 to 2 hours have elapsed so as to avoid deformation of the incompletely hardened cast, but, on the other hand, not later, as the hardening may have reached such a degree that minor parts may be broken when the cast is cut off below the great cistern. After the brain has been taken out of the calvarium, most of the soft tissue is removed manually; the cast, with whatever remains, is placed in 70 % sulphuric acid for some days, after which it is washed in water and finally in benzine to remove any fatty matter. The model made by this technique has proved to be of great help in interpreting encephalographies.

It should be mentioned that vessels and nerves show as canals and lacunae in the cast of the ventricular and cerebral fluid systems. Canals are made by the fasciculi optici, the oculomotor nerve, and the internal carotid artery, and lacunae by the trigeminal nerve and the auditory nerve.

The original topographic conditions can hardly be changed by the process, as the systems are drained and injected in situ with an intact

dura mater. Perfect filling conditions with fractionated exchange of fluid with plastic material are, unfortunately, not achievable.

The vessels of the brain can be filled with the plastics material from the carotid and vertebral arteries in the neck. The volume of plastics material required amounts to 75 ml. The vessels should preferably first be washed out with saline in order to eliminate gas bubbles and blood clots which might cause defects. A cast of such delicate structures is, however, most fragile and must be handled with great care. After removal from the calvarium the complete brain should be placed for about 12 hours in a low-percentage formaline solution to which some glycerine has been added in order to make the preparation float and diminish the risks of damage. The brain is then placed in the usual corrosive solution without manual dissection for about a week.

The technique described may, of course, be used in any field of macroscopic anatomical casting. BARTLEY (e. g. 1958) and I have made simultaneous casts of the pelvic arteries and veins in different colours and by this method have been able to demonstrate and explain some normally occurring impressions in these vessels.

Bronze copies of the original mould have been produced by H. Bergman AB, Stockholm, who specialize in casting sculptures, and they are available from the author.

SUMMARY

The history of anatomic moulding is surveyed. A high molecular polyester, Soredur, has proved to be an excellent modern material for this purpose. The technique of filling the vessels and cerebral fluid systems of the brain with this substance is described.

ZUSAMMENFASSUNG

Ein historischer Überblick über anatomische Modellierungsmethoden wird vorgelegt. Es hat sich gezeigt, dass ein hochmolekularer Polyester, Soredur, für diesen Zweck ein ausgezeichnetes Material darstellt. Die Füllungstechnik der Gefässe und des mit Liquor gefüllten Systemes des Gehirns mit dieser Substanz wird beschrieben.

RÉSUMÉ

L'auteur fait l'historique du moulage anatomique. Un polyester de poids moléculaire élevé, le Soredur, s'est montré être un excellent produit moderne pour cet usage. L'auteur décrit la technique d'injection des vaisseaux et des espaces liquidiens cérébraux au moyen de cette substance.

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ANGIOGRAPHIC DEMONSTRATION OF A TUMOR THROMBUS IN THE POPLITEAL VEIN

Report of a case

by

C. Lagergren, Å. Lindbom and *G. Söderberg*

It may be demonstrated by means of arteriography that malignant tumors of mesenchymal origin often contain considerably more blood vessels than the surrounding tissues. The contrast medium is shunted from arteries to veins through wide, irregular vessels in the tumor so that the drainage veins are filled more rapidly and completely than other veins; in many cases these tumor draining veins are already seen in an early phase of filling when a considerable part of the contrast material still remains visible in the arteries (DOS SANTOS, and others). Such hypervascularization with the consequent increased opacity of the tumor tissue may sometimes be so marked that the tumor can be well defined from surrounding normal tissues, and notwithstanding the fact that many of the individual blood vessels in the neoplastic tissue may be of such small calibre that they cannot be identified as distinct vessels (LAGERGREN et coll.). The combination of hypervascularization, shunting, and increased opacity due to many small contrast-filled pathologic vessels has recently made possible an angiographic diagnosis of a tumor thrombus.

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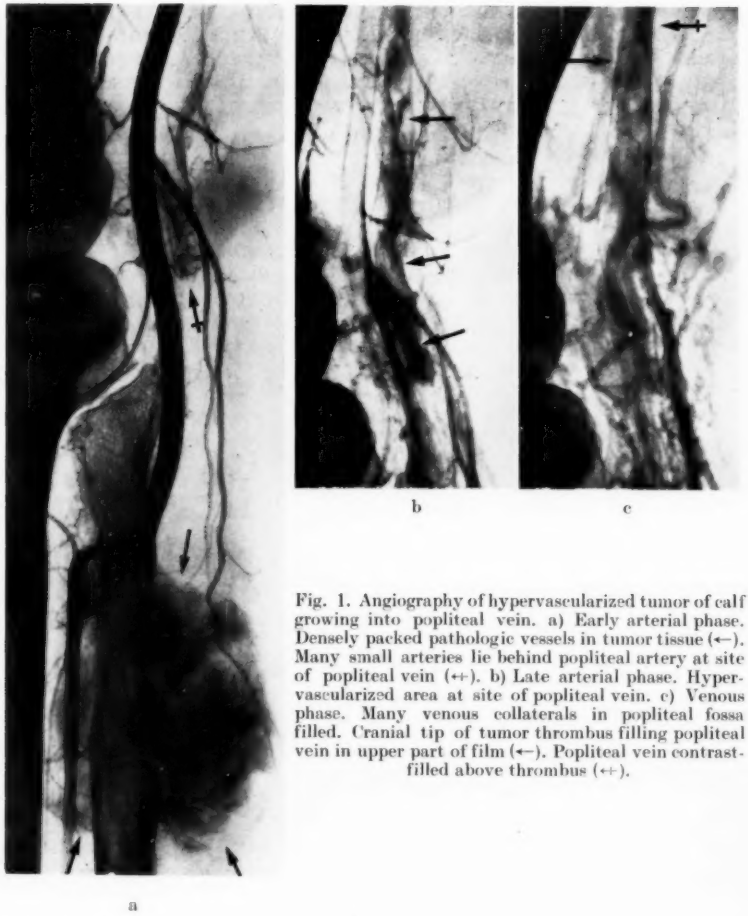
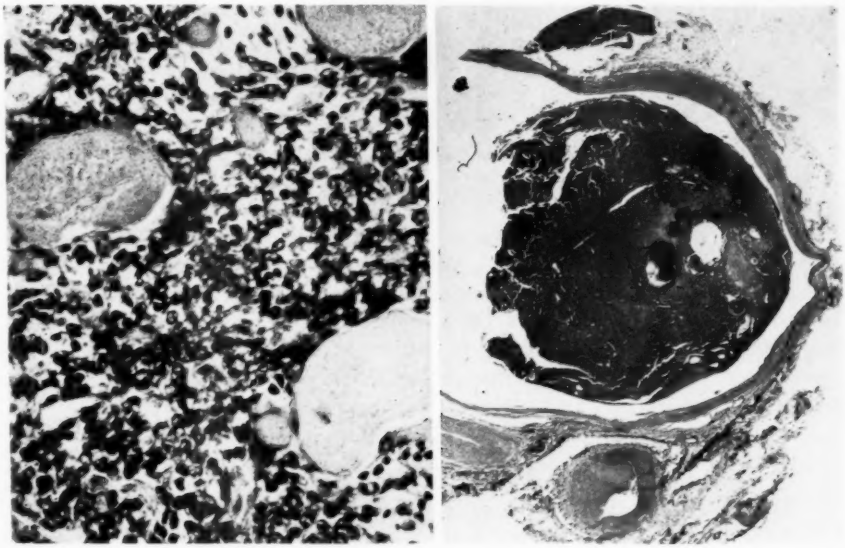


a b c

Fig. 1. Angiography of hypervascularized tumor of calf growing into popliteal vein. a) Early arterial phase. Densely packed pathologic vessels in tumor tissue (←). Many small arteries lie behind popliteal artery at site of popliteal vein (↔). b) Late arterial phase. Hypervascularized area at site of popliteal vein. c) Venous phase. Many venous collaterals in popliteal fossa filled. Cranial tip of tumor thrombus filling popliteal vein in upper part of film (←). Popliteal vein contrast-filled above thrombus (↔).

Male, aged 44, had been treated with irradiation followed by local excision for a moderately well differentiated fibrosarcoma of the calf, and 4 years later had a recurrence at the same site. A tumor was palpable on the dorsal aspect of the lower leg below the popliteal fossa, and roentgen examination showed bony destruction of the fibula. Angiography was performed with Urografin 60 %, and serial films were obtained at approximately 2 second intervals. As early as the first film, taken during the injection, a dense conglomeration of irregular vessels within the tumor were filled, and a fine network of thin, irregularly orientated vessels was observed in the soft parts 5 to 15 cm cranial to the tumor and dorsal to and closely related to the popliteal artery (Fig. 1a). Tissue in a long narrow region behind the popliteal artery and cranial to the tumor was diffusely opaque in the second film of the series (Fig. 1b). The contrast medium was shunted rapidly

Fig. 2. Microarteriogram of a 5 mm thick transverse section through tumor thrombus. Irregularly hypervascularized malignant tissue.



a b

Fig. 3. Photomicrographs of tumor thrombus. a) Poorly differentiated fibrosarcoma with many wide thin-walled contrast-filled vessels. b) Thrombus in popliteal vein.

through the tumor vessels over into the veins and in the third serial film many veins were seen in the popliteal fossa; the popliteal vein itself was, however, not filled in the region between the tumor and a point approximately 10 cm cranial to the upper end of the tibia. The vein was filled above this level but at the lower end of the column of contrast medium there was a rounded defect apparently caused by a mass projecting upwards from below; a thin layer of contrast medium lay along the wall of the vein in this region (Fig. 1c). On examination of the series of films, it was apparent that the diffusely opaque tissue evident in the first film corresponded to the filling defect noted in the third film in the series, and the head of the defect extended to a level 15 cm cranial to the tumor. The filling defect appeared to be caused by a recent thrombus.

Barium emulsion (Micropaque) was injected into the popliteal artery following amputation of the limb. The specimen was then dissected, and it was found that the tumor had grown mainly in the lateral gastrocnemius muscle on the posterior aspect of fibula and tibia; it had invaded the interosseous membrane and partly destroyed the fibula. The growth encircled the nerves and vessels and penetrated into the popliteal vein; the neoplastic tissue was partly adherent to the wall of the popliteal vein but its upper end lay free in the lumen. The tumor and the popliteal vein with surrounding tissues were fixed in formalin and examined by microangiographic and histopathologic techniques. The microangiograms demonstrated rich and similar vascularization of both the main growth and the tissue in the popliteal vein (Fig. 2). The histologic sections revealed the growth to be a poorly differentiated fibrosarcoma and thus of a higher malignancy than the original tumor. Many thin-walled vessels, some attaining a diameter of more than a millimetre, were observed in the tumor tissue (Fig. 3a). Several large veins in the popliteal fossa were crowded with this malignant tissue, and the filling defect in the popliteal vein corresponded to the cranial part of the tumor thrombus with the same histologic appearances as the main tumor (Fig. 3b).

Conclusion

A poorly differentiated fibrosarcoma in the calf grew into veins, and a tumor thrombus in the popliteal vein extended cranially 15 cm from the primary tumor. Contrast filling of many fine pathologic vessels in the poorly differentiated tissue of the tumor thrombus produced diffuse opacity of this thrombus in an early film of the serial angiography. The marked shunt through the tumor caused the veins in the region to be filled to such an extent that the tumor thrombus itself was seen in subsequent films as a filling defect in the popliteal vein. The previous hypervascularization at the site of this filling defect suggested that the thrombus consisted of neoplastic tissue.

SUMMARY

The diagnosis of a tumor thrombus growing into the popliteal vein was made angiographically in a case of fibrosarcoma of the calf.

ZUSAMMENFASSUNG

Die Diagnose eines in die Vena poplitea hineinwachsenden Tumor-Thrombus ist angiographisch beim Fibrosarkom einer Wade gestellt worden.

RÉSUMÉ

L'angiographie a permis de faire, dans un cas de fibrosarcome du mollet, le diagnostic d'un thrombus tumoral proliférant dans la veine poplitée.

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FROM THE DEPARTMENT OF RADIOTHERAPEUTICS (DIRECTOR: PROF. J. S. MITCHELL), UNIVERSITY OF CAMBRIDGE, ENGLAND

EFFECT OF SENSITIZING AND PROTECTING COMPOUNDS IN ROENTGEN IRRADIATION OF LYMPHOCYTES IN VIVO

by

G. H. Hjort

It has been shown that medication with certain sulphur-containing compounds, such as cysteine and cysteamine, prior to roentgen irradiation can afford protection in animals.

BACQ and HERVE (1951) reported that methylamine was able to protect mice against roentgen doses smaller than 850 r. They also reviewed (1954) the protective action of many compounds and found that a large number of amines protect mice against whole-body irradiation, and the best effect was obtained with cysteamine. Similar experiments on the protection of mice and rats against whole-body irradiation were carried out by LANGENDORFF, KOCH and SAUER (1954). These authors investigated a series of sulphur-containing compounds and found that cysteine, cysteamine, thiourea, and many substituted cysteine and cysteamine compounds offered a protective effect; they concluded that this effect was related to the basic formula:

$$HS-(CH_2)_x-N^{R_1}_{R_2}$$

Another group of sulphur-containing compounds, the dithio-carbamates and substituted derivatives, has been studied by VAN BEKKUM, and

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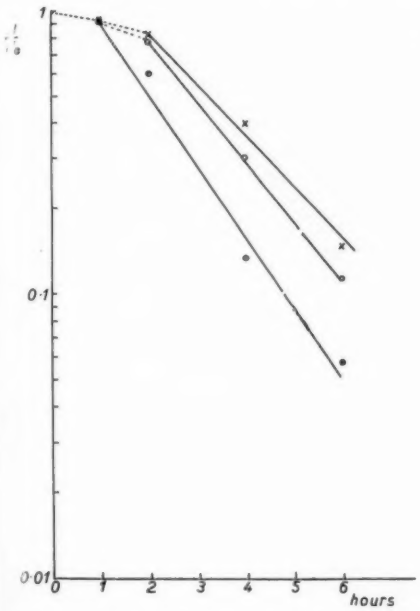

Diagram 1. Time-effect curves after irradiation and, respectively, after irradiation with previous injection of cysteine.

⊙——⊙ 600 r
o——o 600 r + 45 mg cysteine 30 min before irradiation
x——x 600 r + 45 mg cysteine 3 min before irradiation

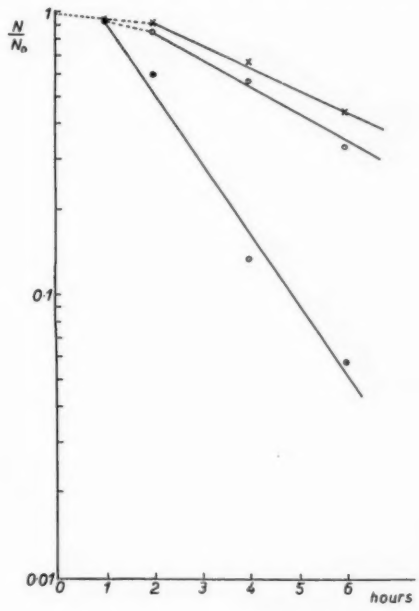

Diagram 2. Time-effect curves after irradiation and, respectively, after irradiation with previous injection of cysteamine.

⊙——⊙ 600 r
o——o 600 r + 23 mg Becaptane 3 min before irradiation
x——x 600 r + 23 mg Becaptane 15 min before irradiation

Abscissa: Time in hours. Ordinate: Fraction of surviving cells.

a number of these were found to have a protective effect against whole-body irradiation in mice.

In all these experiments lethality has been taken as the criterion of the roentgen effect. The influence of roentgen protectors on single cells has been studied by FORSSBERG and NYBOM who showed that cysteine reduced the incidence of chromosome aberrations in onion-root tips after irradiation. Both cysteine and cysteamine (DEVIK 1954 and 1955) were shown to offer a protective effect on chromosome aberration in bone marrow cells and the effect was increased under hypoxia. PATT et coll. reported that the sensitivity of the thymocytes of rabbits irradiated in vitro decreased by a constant factor over a wide dose range when cysteine was added to the suspension.

Table 1

Pycnotic counts of lymphocytes taken from a cervical node in rat

Treatment	Half-value time $\frac{T}{2}$ hours	Mean survival time τ hours	Number of undamaged cells per 1 000 counted at specified hours after irradiation			
			1 hour	2 hours	4 hours	6 hours
600 r	1.30	1.89	905	609	135	58
Cysteine 3 min before irradiation with 600 r	1.70	2.46	903	826	409	151
Cysteine 30 min before irradiation with 600 r	1.45	2.10	928	782	300	115
Becaptane 3 min before irradiation with 600 r	4.70	6.67	947	847	572	332
Becaptane 15 min before irradiation with 600 r	4.45	6.45	955	930	667	437
300 r	2.25	3.26	937	759	399	175
150 r	5.45	7.89	959	858	684	513
Synkavit 30 min before irradiation with 150 r	4.40	6.36	913	878	624	461
Synkavit 30 min before sham irradiation			959	954	930	893
Sham irradiation			967		963	966

Table 2

Cell counts 6 hours after the respective irradiations

Dose	Irradiation		Becaptane 15 min before irradiation	
	% damaged cells	Probit	% damaged cells	Probit
75 r	18.2	4.09	12.3	3.84
150 r	48.7	4.97	22.7	4.25
300 r	82.5	5.93	28.6	4.43
600 r	94.2	6.57	56.3	5.15
1 200 r	98.2	7.10	66.7	5.43
	LD_{50}		LD_{50}	
	155 r $\pm$ 3.8 r		530 r $\pm$ 36 r	

It has been shown that 1—4 naphthoquinone (synkavit) has a radiosensitizing effect on tumour tissue (MITCHELL 1955) and chick fibroblast culture (MITCHELL and SIMON-REUSS); the latter stated that synkavit also had an antimitotic effect. In lower forms of life, synkavit failed to produce any effect of radiosensitivity upon the organism investigated (KOHN & GUTER).

The pycnotic count of lymphocytes taken from a cervical lymph node in a material of rats was used in the present investigation. The details of the technique were described in a previous paper (HJORT 1959). In an attempt to modify the irradiation effect, cysteine, becaptane, or

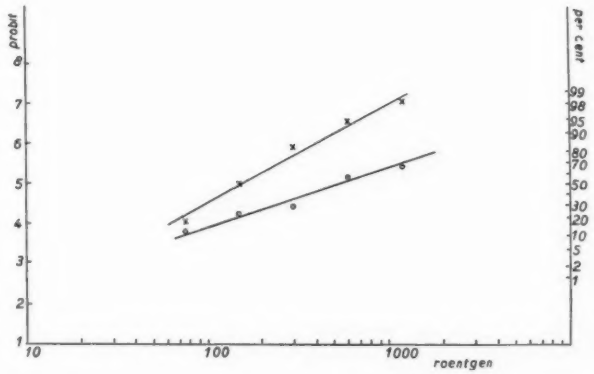

Diagram 3. Dose-effect curves after irradiation and, respectively, after irradiation and previous injection of cysteamine.

x ———————— x 6 hours after irradiation
o ———————— o 6 hours after irradiation and injection of Becaptane 15 min before the irradiation

Abscissa: Dose in roentgen. Ordinate: Percentage damaged cells.

synkavit were injected into a tail vein of the rats before irradiation, the time interval between the injection and the commencement of the irradiation varying between 3 and 30 minutes.

Results

Protecting compounds. A dose of 45 mg of cysteine was given 3 or 30 min before irradiation with 600 r. A slight protective effect was produced, this being best when the preparation was administered 3 minutes before irradiation. The time-effect curve (Diagram 1) showed a prolongation of the latent period to 2 hours and a slight increase in the subsequent mean survival time when the cysteine was given 3 min before the roentgen dose but that the cysteine effect was only a prolongation of the latent period when the substance was administered 30 min before irradiation (Table 1).

Becaptane (cysteamine) was employed in doses of 23 mg and administered 3 or 15 min before irradiation. Becaptane injected 3 min before irradiation had a much more marked effect than cysteine given 3 min before irradiation, and becaptane injected 15 min before irradiation was still more effective. The time-effect curve (Diagram 2) in this case followed quite a different course from the control 600 r curve, the mean survival time of the cells being increased to a value near the figure found for 150 r (Table 1). There was consequently a definite protection of the cells

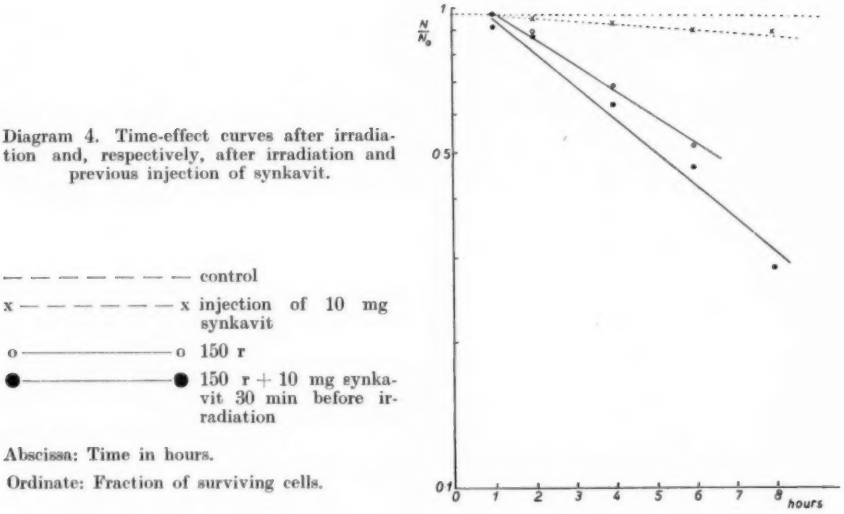

Diagram 4. Time-effect curves after irradiation and, respectively, after irradiation and previous injection of synkavit.

— — — — — — — control

x — — — — — — x injection of 10 mg synkavit

o ——————— o 150 r

● ——————— ● 150 r + 10 mg synkavit 30 min before irradiation

Abscissa: Time in hours.

Ordinate: Fraction of surviving cells.

against the radiation. To investigate this point further the dose-effect curve (Diagram 3) was worked out and the LD_{50} dose calculated (Table 2) (FINNEY). It was found that becaptane offered protection by increasing by a factor of 3 the dose necessary to kill 50 per cent of the cells.

BACQ (1954) investigated the lymphocyte decrease in the peripheral blood and failed to find any protective effect of becaptane on the decreased lymphocyte level, which seems to be in contradiction to the present findings. However, factors other than viability of the cells may cause a decrease in the number of cells in the peripheral blood. It has been shown by FULTON et coll. that, following irradiation, there is an increased coherence between the leukocytes and between the leukocytes and endothelial cells; from SAVITSKY's experiments, however, it appears that this adherence of leukocytes is not related to the fall in the leukocyte count. SCHECHMEISTER and FISHMAN have reported a decreased ability of leukocytes to migrate within 24 hours after irradiation, and this phenomenon may be independent of the cell viability and might have a considerable effect on the leukocyte level in blood.

Radiosensitizing compound. Synkavit was used in doses known to produce a radiosensitizing effect in tumours (MITCHELL 1955). Synkavit in a dose of 10 mg was injected intravenously 30 min prior to irradiation with 150 r and the animals were killed 1, 2, 4, and 6 hours after irradiation; control animals received the same dose and were killed at corre-

ponding times after the injection. The time-effect curve for the synkavit nd irradiation (Diagram 4) shows a slight decrease in fraction of surviving ells over the corresponding control irradiation curve; furthermore the synavit injection curve indicates a small rise in the pycnotic count which orresponds to the difference between the synkavit irradiation curve and he irradiation curve. The failure of synkavit to produce a radiosensitizing ffect on the lymphocytes when given in doses capable of sensitizing umour cells may be due to the differences in metabolism between umour cells and lymphocytes. A more probable explanation, however, nay be the fact that synkavit and related compounds are present in a igher concentration in tumour tissue than in normal organs (MITCHELL 955).

Acknowledgements

I wish to thank Professor Mitchell for his interest in the work and help with the roblems, and Mr. E. King for his valuable technical assistance. The work has been aided y financial support from the British Council.

SUMMARY

Attempts have been made to influence lymphocyte radiosensitivity by administering radio-protecting or radio-sensitizing compounds prior to whole-body irradiation in rats. Cysteine produced a slight protective effect and a doubling of the latent period; cysteamine gave a threefold increase in the radioresistance of the lymphocytes. Synkavit given in doses capable of producing sensitizing effects on tumour tissue failed to cause any changes in the radiosensitivity of the lymphocytes.

ZUSAMMENFASSUNG

Versuche sind gemacht worden, die Strahlenempfindlichkeit der Lymphozyten bei Ratten durch Gaben strahlenschützender oder strahlensensibilisierender Mittel vor einer Ganzkörperbestrahlung zu beeinflussen. Zystein zeigt eine leicht schützende Wirkung und eine Verdoppelung der Latenzzeit. Zysteamin hat eine dreifache Erhöhung der Strahlenresistenz der Lymphozyten gegeben. Synkavit, das in Dosen gegeben wurde, welche sensibilisierende Wirkung auf Tumorgewebe zeigen, ergab keinerlei Veränderungen der Strahlenempfindlichkeit der Lymphozyten.

RÉSUMÉ

L'auteur a essayé d'influer sur la radiosensibilité des lymphocytes en administrant à des rats, avant irradiation totale, des corps radio-protecteurs ou radio-sensibilisateurs. La cystéine présente un léger effet protecteur et double la période de latence. La cystéamine triple la radio-résistance des lymphocytes. Le synkavit donné à dose sensibilisant le tissu tumoral n'a pas modifié la radiosensibilité des lymphocytes.

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BOOK REVIEWS

STUDIES ON THE EFFECT OF THYROTROPIC HORMONE ON THE THYROID FUNCTION IN MAN. By Jerzy Einhorn. 107 pages, 23 illustrations and 22 tables. Acta radiol. (1958). Suppl. No. 160. Price: Sw. Kr. 30: —.

A functional relationship between the thyroid gland and the hypophysis has long been recognized, and the thyrotropic hormone (TSH, thyrotropin) has been used in clinical practice since the introduction of radioiodine for the detection and treatment of thyroid disorders. Our knowledge of this relationship is, however, imperfect and the mechanism of the action of TSH on thyroid function is obscure. The aim of this investigation was to study the action of TSH in varying doses upon the iodine metabolism in the thyroid, as well as the relationship between the time of TSH administration and the effect of the latter on the thyroid function.

The communication deals in the main with the effects of single injections of TSH on the thyroid function in patients without thyroid disease. Time- and dose-response relations were studied in relation both to the hormone release from the gland and to its uptake of radioactive iodine.

Time-response relations for the uptake were investigated by means of I^{132} (half-life 2.3 hours) which made repeat tests in the same subject possible at short intervals. The radioiodine accumulating capacity of the gland started to increase after a latency of 8 hours following a single intramuscular injection of TSH. It reached its maximum 18 to 24 hours after the injection and then gradually decreased. From 8 to 18 days following the injection a rebound phenomenon was observed; the radioiodine accumulation rate was at first lower than the pre-TSH level, then returned to approximately the original value.

Protein-bound radioiodine (PBI^{131}) in serum was used in studying the time-response relations for hormone release. The results indicated that this release was already influenced within the first 90 minutes, and that the effect continued to increase for at least the first four hours after the injection of TSH (0.3 USP units per kilogram bodyweight). The release per unit time was higher than the original rate for not less than 24 hours.

Studies of the dose-response relations for radioiodine accumulation in the gland were based on one test which reflected its initial accumulation rate after an intravenous injection, and on the conventional 24-hour thyroid uptake and the urinary excretion of radioiodine. Protein-bound iodine (PBI) in plasma was used in studying the dose-response relations for hormone release. One hundred and seventy patients were divided into groups which were tested with single doses of TSH of from 0.003 to 0.2 USP units per kg/bodyweight. As regards the thyroid response to stimulation with mounting doses of TSH, the maximum effect on the radioiodine uptake was obtained with much

smaller doses than those required for the maximum effect on the release of organic iodine. The influence of age, sex, and weight factors upon the response to a single injection of thyrotropin is analyzed, and the incidence of clinical signs following varying doses of TSH is discussed.

The last section contains some findings relating to the effect of TSH in hyperthyroid subjects. In most cases of exophthalmic goiter a single injection of 0.05 to 0. USP units per kilogram bodyweight caused a substantial rise in the initial accumulation rate of radioiodine, but the changes in the 24-hour thyroid uptake were indefinite. When the previously reported time-response relations observed in euthyroid subjects were applied in a series of patients with low radioiodine uptakes despite unquestionable hyperthyroidism, TSH caused a marked though transient elevation of the uptake. Most of these patients had toxic nodular goiter and/or a history of excessive iodine intake. The observation was utilized for radioiodine therapy.

The total series comprises tests in 710 in-patients. The results were subjected to statistical analyses. Certain physiologic and practical clinical problems are discussed with due regard to the results.

Autoreview

GRUNDLAGEN DER STRAHLENBIOLOGIE. Von Z. M. Bacq und P. Alexander. Deutsche Übersetzung. Herausgegeben von H.-J. Maurer. 396 S., 115 Abb. G. Thieme Verlag, Stuttgart 1958. DM. 49.50.

This is a new edition of the English original which appeared in 1955. Two chapters have been completely rewritten, namely those covering the therapy of animals lethally damaged by radiation through the transfer of bone marrow or cells of the spleen — a field in which spectacular advances have been made in recent years. The chapter on the influence of oxygen in radiation biology has also been brought up to date. The book is otherwise essentially a translation of the first English edition and stands as the sole comprehensive survey of radiobiology and adjacent fields. Nearly 1 000 papers are quoted, which indicates the great amount of experimental research work which has been included.

After a short presentation of certain physical data a comprehensive presentation of the effects of ionizing radiation on chemical systems is given. Radiation chemistry has greatly promoted the understanding of the biologic effects of irradiation. The chemical effects of ionizing radiation in aqueous solutions of simple salts, the direct and indirect action of radiation, the influence of oxygen, the effects of radiation on organic macromolecules are all instructive subjects for the biologist and the physician.

The biologic part of the book is subdivided on generally accepted lines. The important question of the action on the cell nucleus and the chromosomes as well as the cytology of these phenomena are adequately treated although the genetic effects are only just touched upon. Further chapters are devoted to the vast experimental material on various physiologic and biochemical irradiation effects, a difficult field due to the partly contradictory experimental evidence. Chemical protection against radiation and the therapy of irradiation damage is well treated. A chapter on certain human data completes a book which in an admirable way covers this huge and diverse material in a volume of only about 400 pages. A large number of figures and tables as well as a subject index facilitates its perusal.

A. Forssberg

L'Angiographie Cerebrale. Par Joël Bonnal et Jaques Legré. 254 p. 223 ill. Masson Editeurs, Paris 1958. 6 000 fr.

According to the preface the authors do not claim to add anything new to our knowledge of cerebral angiography. Their aim is rather to give, for the first time in the French language, an exposé as simple and clear as possible, which can act as a basis for making a correct angiographic diagnosis. In this their intention they have certainly been successful. Without being lost in details they give a clear description, easy to survey, of the different technical methods, the normal anatomy and physiology of the cerebral circulation and changes caused by various lesions, such as tumours, haematomas, vascular malformations and occlusions. Their description seems to be based mainly on a thorough study of the literature. From the critical way in which this is performed it is however apparent that the authors have a good knowledge and much experience in neuroradiology. This is also evident from the illustrations, which are well selected, in most cases well documented, and of excellent quality. Most of the illustrations are reproductions of angiograms, but some schematic drawings and diagrams are also included.

A few critical remarks could perhaps be made: In Fig. 7, both the anterior and the posterior cerebral artery is marked with 3, apparently by mistake. It is somewhat surprising to find that the 'kystes hydatiques' are mentioned together with the 'gros kystes gliomateux' as tumours giving a typical picture of avascular lesions. When the authors characterize angiography as an examination 'sans danger, sauf chez les grand artérioscléreux et les grand hypertendus artériels' they are, in the reviewer's opinion, going rather far in their enthusiasm. On the whole, however, the book can be highly recommended as an introduction in cerebral angiography, and useful also for trained neuroradiologists.

Ingmar Wickbom

BOOKS RECEIVED

We acknowledge with thanks under this heading books received for review, which we trust will be regarded as a sufficient mark of appreciation of the courtesy of the sender. The reviews of selected items will appear as soon as opportunity affords.

Symposium Über schädliche Wirkungen schwacher Strahlendosen. Benno Schwabe & Co., Basel 1958.

The Sella in Health and Disease. The value of the radiographic study of the sella turcica in the morbid anatomical and topographic diagnosis of intracranial tumours. By Mahmoud el Sayed Mahmoud. British Journal of Radiology. (1958). Supplement No. 8.

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Year Book of Radiology 1958—1959 Series. Year Book Publishers, Chicago 1959.

X Ray Diagnosis of the Alimentary Tract in Infants and Children. By Edward B. Singleton. Year Book Publishers, Chicago 1958.

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GENETICS, RADIOBIOLOGY AND RADIOLOGY PROCEEDINGS, Mid-Western Conference. Charles C. Thomas, Springfield, Ill., 1959.

ANGIOCARDIOPNEUMOGRAPHIE ÉLARGIE. Méthode d'opacification vasculaire générale par voie veineuse. Par P. Viallet, L. Sendra, L. Chevrot, P. Aubry et P. Combe. Masson et Cie, Paris 1959.